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'N.M.R.INVESTIGATIONS OF BICYCLIC

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CONTENTS

SUMMARY

^{13}C Chemical shifts of 4-substituted tricyclenes, 4-substituted camphors, 1-substituted camphenes and the ^{15}N chemical shifts of diazoalkanes are discussed in terms of correlations with Hammett-type parameters, C.N.D.O./2 calculations, steric effects and with the chemical shifts of similar compounds.

The β -chemical shifts of the camphenes, camphors and tricyclenes are rationalised by estimating distances of the β -carbon to substituent atoms and relating the shifts to the magnitude and direction of the expected 1, 4 and 1, 5 effects.

The contribution of field effects to the total chemical shift of carbons is considered, and the correlation of C(2) chemical shifts in camphenes and camphors with linear free energy parameter, σ_I, is taken as indicating a significant contribution from field effects at these carbons.

^{15}N chemical shifts of diazoalkanes appear to be affected by changes in both the mean excitation energy, ΔE, and the electron density.

Dual Substituent Parameter (D.S.P.) correlations of the S.C.S. and electron densities of meta and para-substituted, 1′ , 1′ , 1′ trimethylammonio 2′ -benzimides, 1′ , 1′ dimethyl 2′ -benzoylhydrazides and acetophenones provide a means of examining electronic transmission in these series. In addition, it is shown that inclusion of a contribution from bond order to the effective electron density accounts for the shift changes observed at the carbonyl carbon.

Extended or reduced conjugation between the benzene ring and a $O = \overset{\beta}{C} - \bar{N} - \overset{+}{N}(Me_3)$ group does not appear to alter the mechanism of electronic transmission to the carbonyl carbon, as monitored by the ^{13}C chemical shifts of para-substituted 1′ , 1′ , 1′ trimethylammonio 2′ -cinnamimides and 2′-phenylacetimides, although in the latter case electronic

transmission to the carbonyl carbon is severely reduced.

Long range proton-proton couplings between $H_{3\ exo}$ and $H_{5\ exo}$ in 4-substituted camphors and their nitrimines are shown to correlate with σ_I and the nitrimine shows diminished values with respect to the parent ketones. From this it is tentatively suggested that the carbon-nitrogen double bond in nitrimines is less polar than the carbonyl bond.

INTRODUCTION.

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY[1,2]

Nuclear magnetic resonance (n.m.r.) spectroscopy is one of the most widely used techniques in chemstry and, whereas most laboratories now have their own facilities for obtaining n.m.r. spectra, before 1950 n.m.r. held little interest for chemistry. The discovery that the precise resonance condition for a given type of nucleus depends on its chemical environment opened new fields of research. In 1951 separate absorption bands were resolved for chemically different protons in the same molecule.[3] This led to the term chemical shift to describe the difference in resonance conditions required for the same isotope in different environments. With this development, n.m.r. became one of the most important tools in the study of molecular structure.

All nuclei with odd mass numbers possess angular momentum, magnetic moments and have spins of value I, where I is an odd integral multiple of ½. The maximum observable component of the angular momentum is I, the spin quantum number, and the permitted values of vector moments along any axis are given in terms of the magnetic quantum number, m, where

$$m = I,\ I - 1, \cdots, 1 - I,\ -I$$

The magnetic moment, $\mu = \gamma \frac{I h}{2\pi}$

where h = Plancks' constant

γ = the magnetogyric ratio

There are 2I + 1 possible orientations or spin states for a given nucleus. In the absence of a magnetic field, the states are degenerate. When a magnetic field is applied, degeneracy is lifted and these states correspond to different potential energy levels.

Nuclear magnetic resonance spectroscopy is concerned with the detection and measurement of transitions between spin states.

THE N.M.R. EXPERIMENT.

This experiment considers the effect of an applied magnetic field on an array of magnetic nuclei with spin e.g. ½.

A magnetic moment, μ, lies at an angle, θ , to the field axis (z axis) of the magnetic field, H_0. The interaction of H_0 and μ causes the nucleus to precess about the z axis with angular frequency, υ_0 , where

$$\upsilon_0 = \frac{\gamma}{2\pi} H_0 \quad \text{(Larmor equation)}$$

The spinning motion of the nucleus does not cause θ to change and the angular frequency is independent of θ . The energy of the system, $E = -\mu H_0 \cos\theta$ and thus depends on the value of θ .

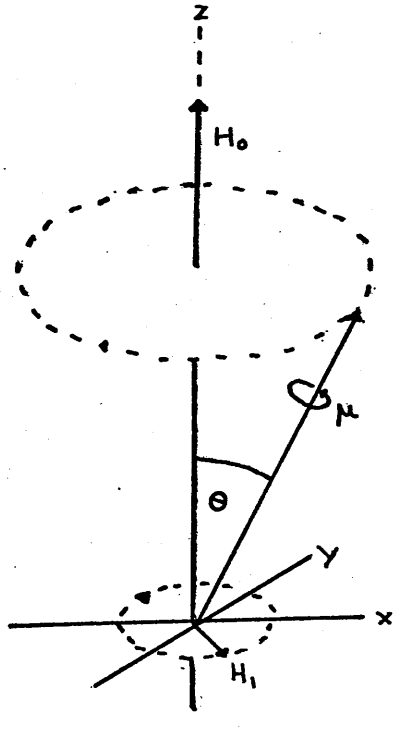


fig.1

If a small rotating field, H_1, is generated orthogonal to H_0, μ experiences the combined effects of H_0 and H_1, if H_1 rotates with frequency υ_0 . Under these conditions θ changes as the nucleus absorbs energy from H_1.

If θ does not change H_1 will not remain in phase with μ and energy will not be transferred to the nucleus. The condition for resonance is that at which energy is transferred. The usual method of producing rotating H_1 fields is to pass an oscillating radio-frequency (r.f.) signal through a coil whose axis is orthogonal to the H_0 axis.

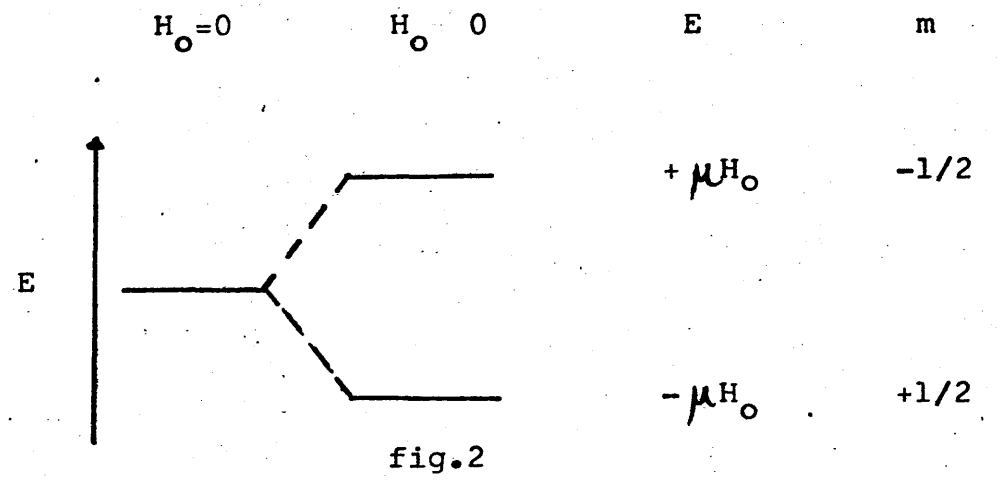


fig.2

The above classical approach for the interaction of H_0 and μ may be expressed in the quantum mechanical statement,

$$h\upsilon = \mu \frac{H_0}{I} = \Delta E$$

where ΔE is the energy separation between adjacent nuclear spin states as in fig.2. For nuclei with spin ½ only two states are possible and they have an energy difference of $2\mu H_0$, which corresponds to only a few millicalories per mole.

The relative populations of these states are given by

$$\frac{N_+}{N_-} = \exp \frac{-\Delta E}{k T}$$

where N_+, N_- are the populations of the upper and lower energy states respectively.

The equilibrium excess population in the lower state, n_{eq}, is given by

$$n_{eq} \approx \frac{2 \mu H_0}{k T}$$

The excess population which can be maximised by

increasing the field,causing a small moment directed along H_0. This small excess of nuclei (<1 in 10^5) gives rise to an observable n.m.r. signal.

At the resonance frequency, υ_o , energy can be transferred between the two levels.

The probabilities of transition are proportional to the populations of the two energy levels and, therefore, the probability of an upward transition is slightly greater than the probability of a downward transition.

In n.m.r. experiments a slow sweep rate is used causing H_1 to pass slowly through the resonance condition and therefore while excitation is occurring, the energy level populations may equalise. If this occurs, no further absorption is observed and the sample is said to be saturated.

NUCLEAR SPIN RELAXATION.

The process whereby an array of identical nuclei, which are not being irradiated, in either the upper or lower energy state return to their Boltzmann distribution is termed Relaxation.

The transitions between spin states in n.m.r. occur in the radio-frequency region of the electromagnetic spectrum. There is no spontaneous emission of energy at these frequencies, such as that which occurs in the ultra violet and infra red regions. Therefore excited nuclei must utilise other mechanisms to return to their ground states.

The redistribution of the populations of the two energy levels must arise from an interaction of the nuclei with their surroundings, known as the lattice, which for a liquid is taken as the rotational, translational and other degrees of freedom of the molecular system. This process is spin lattice relaxation. It is a non-radiative transfer of energy and occurs by a first order rate process characterised by a lifetime, T_1, which is given by $\frac{1}{k}$ where, k , is the rate constant for the process. T_1 is the time required for the difference between the excess spin population and its equilibrium value to decrease by the factor e.

The spin lattice relaxation time, T_1, is also known as the longitudinal relaxation time as it measures the time for

the magnetization to decay in the direction of the field axis (see fig.1). The value of T_1 for a specific nucleus depends on the isotope, its chemical environments, and the physical state of the sample. For liquids T_1 is usually in the range 10^{-2} - 10^{2} sec.

The time for the magnetization to decay in the x , y plane (see fig.1) is called the transverse relaxation time or spin-spin relaxation time, T_2.

SPIN-LATTICE RELAXATION.

There are several interaction mechanisms which can bring about the relaxation of different systems. In each mechanism the relaxation is caused by fluctuating, localised magnetic or electric fields in the sample resulting from molecular motions. There are several ways in which molecular motions can give rise to fluctuating local magnetic fields, the important ones being:

1) Fields due to the magnetic moments of other nuclei.
2) Fields due to the spins of unpaired electrons.
3) Fields due to variable electronic screening of the static field H_0 (intra or intermolecular).

For nuclei with spin $I > \frac{1}{2}$ nuclear electric quadrupole moments can interact with variable electric fields coupled to the other degrees of freedom. This leads to electrical relaxation as an additional mechanism.

In ^{13}C n.m.r. the most important types of spin - lattice relaxation are dipole-dipole, spin rotation, chemical shift anisotropy and scalar relaxation. For carbon atoms bearing protons dipole-dipole relaxation is the most important mechanism.

This type of relaxation is caused by nuclei which have $I \neq 0$. If two neighbouring nuclei are placed in a magnetic field H_0 the total magnetic field experienced by one nuclei is H_0 plus the effect of the local magnetic field of the other nucleus. The factors affecting this interaction are the magnetic moments, separation and orientation of the two nuclei relative to H_0.

In a liquid, the nuclei are rapidly changing their relative orientation with respect to H_0. This gives rise to

rapid fluctuations of the total magnetic field by altering the magnetic field between the nuclei. These fluctuations effect the relaxation of the nuclei.

Intramolecular relaxations dominate the relaxation of ^{13}C nuclei so the tumbling of molecules and other rotational motions are the most important motions in the relaxation of this nucleus. The efficiency of the relaxation of carbon atoms by protons, using dipole-dipole relaxation, is determined by two factors

(i) Dipole-dipole relaxation is proportional to the square of the magnetogyric ratio of the nucleus being relaxed and of the nucleus causing relaxation. ^{13}C and ^{1}H nuclei both have high magnetogyric ratios and therefore dipole-dipole relaxation is efficient between these two nuclei.

(ii) It is also proportional to R^{-6}, where R is the internuclear distance between the nucleus undergoing relaxation and the nucleus causing relaxation. The nature of this relationship implies that the efficiency of this process attenuates rapidly with increasing internuclear separation. Thus carbon atoms bearing protons are most easily relaxed and dipole-dipole relaxation dominates the relaxation of these carbon atoms.

The average frequency of a localised fluctuating magnetic field determines its effectiveness in causing spin relaxation. Molecules of different sizes tumble at various rates in solution and it is difficult to dissect characteristic motions from the overall effect. However, it is not necessary to measure the effect of each type of molecular motion and we need only consider the average time for the molecule to rotate through one radian. This is called the effective correlation time, t_c.

The most effective dipole-dipole relaxation occurs at frequencies in the region of the Larmor frequency which is 2.5×10^{7} Hz at 23.5 k.G. or 1.6×10^{-8} rad/sec. for ^{13}C nuclei, corresponding to a correlation time of 7×10^{-9} sec.

The effect of t_c on the magnitude of T_1 is shown in fig.3.

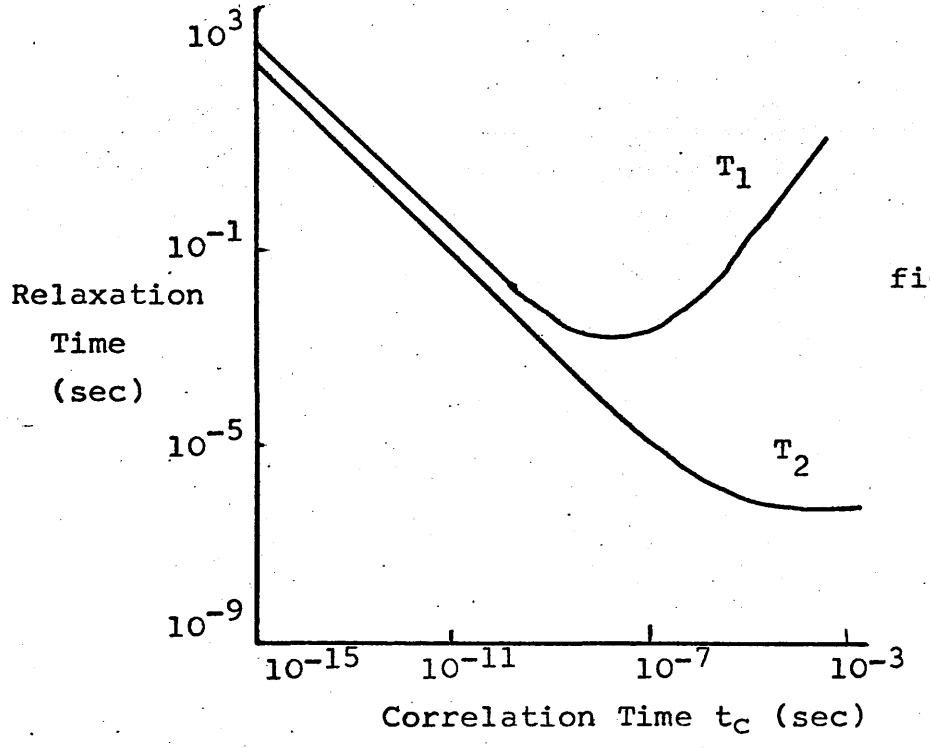


fig.3

fig.3 demonstrates that in the region $t_c < 10^{-8}$ sec. T_1 increases as t_c decreases, whereas when $t_c > 10^{-8}$ sec. T_1 increases with t_c. For medium sized organic molecules (molecular weight, ca. 150) t_c is of the order 10^{-12} - 10^{-13} sec. depending on solvent and temperature. Larger molecules tumble more slowly because of their size and due to increased interaction with solvent molecules. Restricted polymer systems have t_c values approaching the minimum (10^{-9} sec.) in fig.3. Hence large molecules can relax more efficiently than small rapidly rotating molecules.

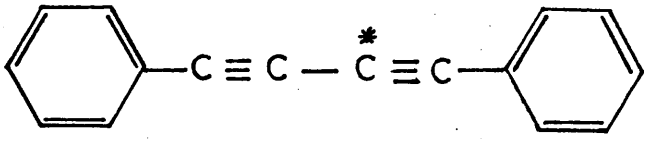
For t_c values greater than 10^{-8} sec., as are found in solid state n.m.r. the situation reverses and molecules which tumble faster relax more efficiently.

The other mechanisms of spin-lattice relaxation become important in certain circumstances.

Spin rotation relaxation (S.R.) is important in small molecules and freely rotating methyl groups which can be relaxed utilising rotational states of the molecule. It some dominates the relaxation of non-protonated carbons and two molecules in which S.R. dominates in the relaxation of ^{13}C nuclei are carbon disulphide and the methyl group of toluene. It is found that for molecules where S.R.

dominates, T_1 decreases as the temperature increases.

Chemical shift anisotropy (C.S.A.) is a fairly rare contributor to the overall T_1. It arises from directional differences in electronic environment of the nucleus which can give rise to fluctuating magnetic fields when the molecule tumbles in solution. The C.S.A. T_1 varies according to the magnetic field strength and a typical carbon atom with significant C.S.A. contribution in its overall T_1 is the carbon atom marked * in the molecule (1).



(1)

Scalar relaxation occurs when a nucleus is spin-spin coupled to a nucleus which is undergoing rapid spin-lattice relaxation, usually by quadrupolar relaxation; this situation is usually confined to nuclei with $I > \frac{1}{2}$. The spin-spin interaction causes a fluctuating scalar interaction between the two nuclei and is a significant contributor to the overall T_1 if the other nucleus is spinning with a frequency close to the Larmor frequency.

This mechanism also contributes to spin-spin relaxation, T_2, and hence nuclei relaxed by this mechanism are usually significantly broadened i.e. ^{13}C coupled to ^{14}N (see next section). The mechanism also dominates the relaxation of $^{*}C$ - Br in bromobenzene.

SPIN-SPIN RELAXATION.

In high resolution n.m.r. the individual transitions give rise to signals approaching their natural linewidths, $\Delta\upsilon$, thus the Heisenberg uncertainty principle is applicable to this system and $\Delta\upsilon \cdot \Delta t \approx 1$.

The life time of the upper state is limited by T_1 thus $\Delta\upsilon$ is expected to be of the order $\frac{1}{T_1}$ which for liquids is about 0.1 - 1 Hz.

It is found that in certain cases line broadening occurs because another relaxation process spin-spin

relaxation, T_2, is the dominant relaxation process. This process arises from the interaction of neighbouring magnetic dipoles.

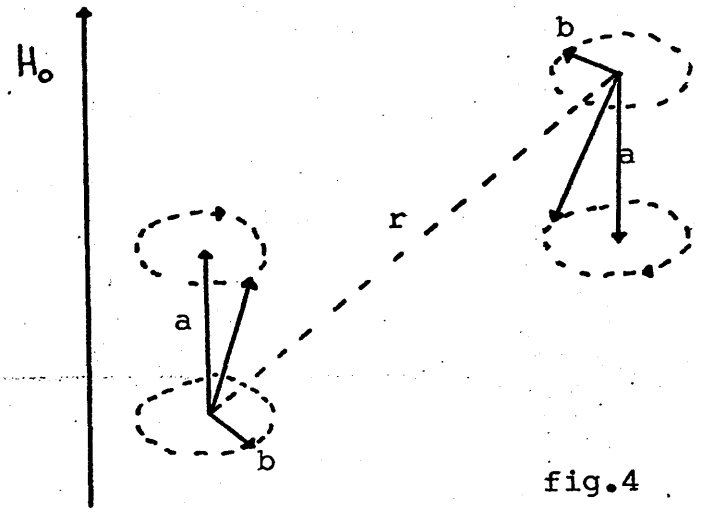


fig.4

If two nuclei precess about the H_0 axis and they lie close together in space they can interact in the following manner. The precessing moment has two components, where in fig.4, (a) is static and aligned with the H_0 axis and (b) is a rotating component precessing in the x y plane. If(b)rotates with a frequency which can cause a spin transition in the neighbouring nucleus, there will be a spin exchange with no change in the total energy of the system, but the lifetimes of the interacting spin states are affected. T_2 is thus concerned with magnetization changes in the x y plane and is called the transverse relaxation time.

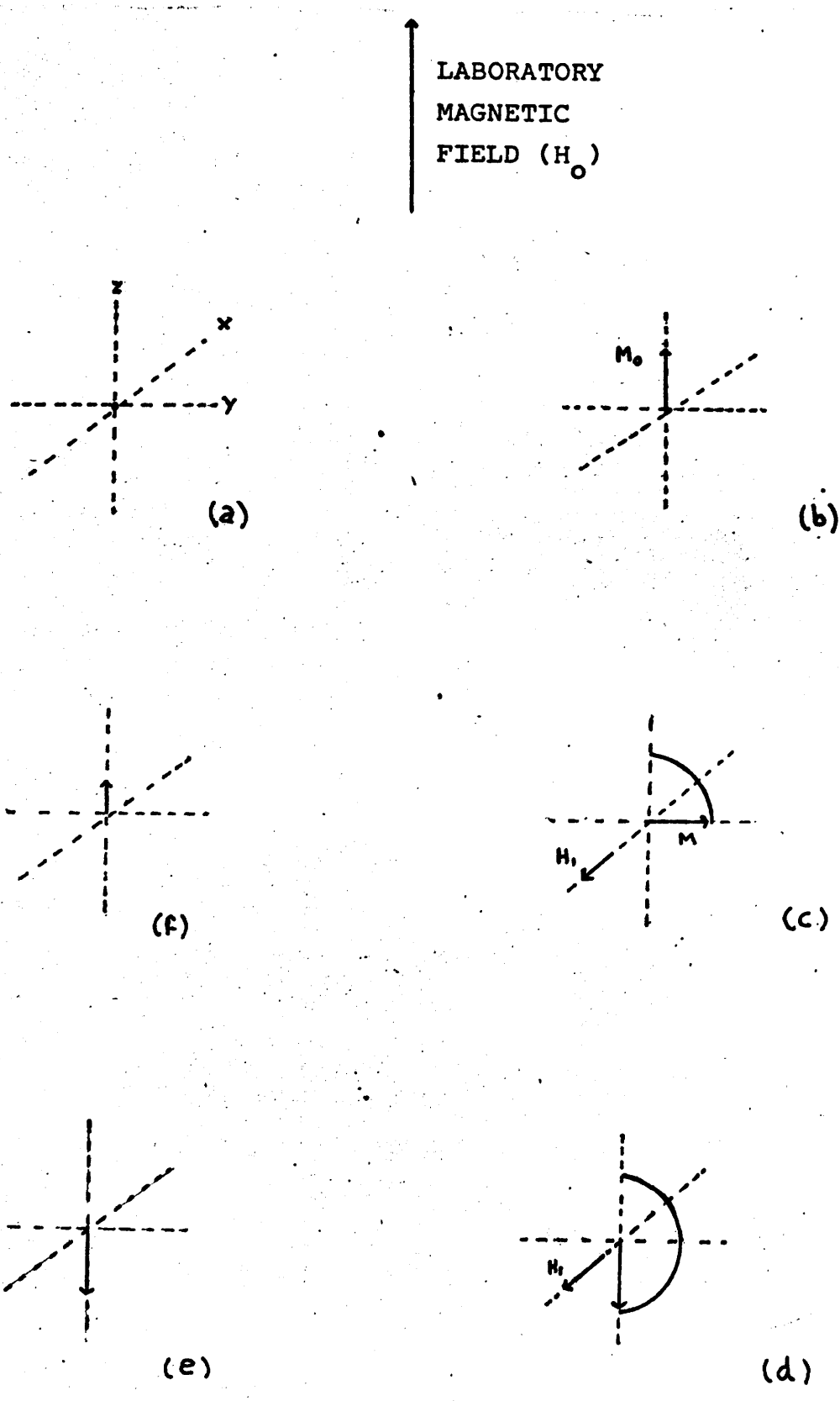
FOURIER TRANSFORM N.M.R.

The sensitivity of n.m.r. signals of protons are 5,700 times greater than those of carbon-13 nuclei in the same magnetic field. This is due to two factors

(i) ^{13}C has only 1.1% natural abundance of the carbon content of a sample.

(ii) the sensitivity of a nucleus in an n.m.r. experiment is proportional to the cube of its magnetogyric ratio. The ratio $\gamma_H : \gamma_C$ is 4 : 1 thus $(\gamma_H)^3 : (\gamma_C)^3$ is 64 : 1.

fig. 5. The pulse n.m.r. experiment in the rotating frame.



In the earlier types of n.m.r. spectrometer the nuclei were scanned by the continuous wave method. This had the disadvantage that only one frequency could be observed at a given time. Rapid sweeps increase the amount of r.f. power which can be used but limit resolution and do not greatly enhance the signal to noise, S/N, ratio.

In order to overcome the inefficiency of single frequency observation methods, all the nuclei in a sample are excited at the same time and the total response of the sample is observed. This is accomplished by applying to the sample a short r.f. pulse, 50 μ sec, which excites a finite bandwidth of frequencies, ca. 5,000 Hz, by nutating the nuclear spins away from their equilibrium orientation with the magnetic field. For this purpose a high power source is required.

THE ROTATING FRAME OF REFERENCE AND THE N.M.R.EXPERIMENT.

This is a simplified method of considering the effect of a series of pulses on an idealised array of magnetic nuclei. In the absence of a magnetic field the sum of all the individual magnetic moments, M, is zero. When the sample is placed in a magnetic field, the nuclei interact with the lattice and an equilibrium excess of nuclei in the lower energy level is established. This causes a small net magnetization, M_0, aligned with the direction of H_0 (z-axis), fig.5(b). When the sample is irradiated by an r.f. field applied along the x axis in the rotating frame, this turns M out of alignment with H_0 and towards the y axis, fig.5(c).

When the field is applied in the form of pulses, the length of the irradiation time determines how far M tips away from the z axis. The time necessary to tip M through 90° must be experimentally determined. If this time, the pulse width, is doubled then the net magnetization tips through 180°, (d). A 180° pulse applied to a fully relaxed system causes a Boltzmann excess to form in the higher energy level. This is called a negative spin temperature.

After any pulse sequence spin lattice relaxation, T_1, occurs in the z direction whereas spin-spin relaxation, T_2, occurs in the x y plane. The n.m.r. spectrometer only detects signals in the x y plane hence no signal is detected after a 180° pulse $\left[(e) \longrightarrow (f) \longrightarrow (b)\right]$. If a pulse is applied at 90° to M_0, M lies in the x y plane. T_1 and T_2 processes can now occur. M moves upwards to M_0 along the z axis and simultaneously the x y magnetization relaxes to zero as a function of T_2. This dephasing process gives rise to the n.m.r. signal and no further signal is observed after the x y magnetization has completely dephased, even if the z axis relaxation is not complete, as occurs when T_1 is greater than T_2.

THE FREE INDUCTION DECAY (F.I.D.)

After an array of nuclei has been excited by irradiation with a short r.f. pulse, the nuclei emit energy at their precession frequencies. The receiver detects this in a pattern called a free induction decay (F.I.D.) which corresponds to the ~~ir~~re radiation of all the frequencies absorbed by different nuclei in the sample, as the spins return to their equilibrium position.

If a sample containing a single type of nucleus is irradiated at its resonance frequency with suitable r.f. power to nutate it through 90°, the F.I.D. will appear as a smooth exponentially decaying curve. If the frequency of irradiation differs from the resonance frequency, the F.I.D. appears as an exponentially decaying sinusoidal curve. The frequency of this sine wave is the difference between the centre frequency of the r.f. pulse and the Larmor precession frequency of the nucleus. If the F.I.D. is recorded for a given period of time the precession frequency (in cycles/sec or Hz) is obtained by counting the number of cycles through which the F.I.D. passes in that time.

The Fourier transform (F.T.) of the F.I.D. is the steady state resonance spectrum. For the case above this corresponds to a single line. The same procedure applies

to more complex situations when more than one energy absorption occurs. The Fourier transform of the F.I.D., in this case, is a series of lines corresponding to the precession frequencies of the individual nuclei and is identical to that which would be obtained by the continuous wave technique.

The time taken for individual frequency components to decay defines the linewidth of each signal and frequencies which decay slowly give the best resolution after Fourier transformation. In general the pulse technique produces spectra with truer linewidths than are obtained by the continuous wave (c.w.) method.

The aquisition of pulsed spectra is seriously limited by the condition that the pulse repetition rate must be greater than the longest T_1, so that the system returns to equilibrium after each pulse. Routinely the interval between pulses is five times the longest T_1 in the sample.

The increased sensitivity of pulsed n.m.r. over c.w. for a single pulse is given by the expression

$$\left[\frac{\text{Total chemical shift range}}{\text{linewidth of the narrowest signal}}\right]^{\frac{1}{2}}$$

This is theoretically about 100 for ^{13}C nuclei although in practice the enhancement from this source is only about 10 fold.

A further improvement over c.w. techniques is obtained in terms of the time needed to obtain a given spectrum. Both methods utilise time averaging to improve the signal to noise, S/N, ratio in a spectrum. For the c.w. method up to several thousand 50 sec. scans can be accumulated, whereas in pulsed n.m.r., ca. 1 million 0.1 sec. pulses can be recorded in the same time. The S/N ratio improves as the square root of the number of scans or pulses, so a given S/N enhancement can be obtained in a much shorter time by pulsing, giving a time improvement of greater than 100.

Further S/N enhancements may be obtained from the Overhauser effect during decoupling.

DECOUPLING OF N.M.R.SPECTRA.

Each carbon in an organic molecule spin-spin couples to any directly bonded protons and those two to four bonds distant. These couplings tend to complicate and impair the resolution of a ^{13}C n.m.r. spectrum of the molecule.

Wide band proton noise decoupling simplifies the carbon spectrum, reducing all the multiplets caused by ^{13}C - ^{1}H spin-spin couplings to singlets by simultaneously decoupling all protons in the sample. This increases the sensitivity due to the simplification of the spectrum and there is also an increase in the S/N ratio as a result of a by-product of decoupling called the Nuclear Overhauser Effect (N.O.E.).[4]

Irradiation of the protons disturbs the population of the upper and lower proton energy levels, and on equalisation of the populations of these levels the ^{13}C proton spin-spin coupling is removed. The carbon nuclei are relaxed by spin lattice relaxation involving dipole-dipole interactions with neighbouring protons. The change in proton energy level populations on irradiation causes a greater excess of nuclei in the lower carbon energy level, at equilibrium, than is expected from the Boltzmann distribution. This increase in population means that the nuclei can absorb more r.f. energy at the resonance frequency and leads to a greater peak area of the signal.

The theoretical increase in peak area for decoupled spectra (I_D) over non decoupled spectra (I_0), the integrated intensity ratio $\frac{I_D}{I_0}$ is 2.988 for ^{13}C,[5] which corresponds to a maximum N.O.E., $\frac{I_D}{I_0} - 1$, of 1.99.[6] Proton bearing carbon nuclei in molecules of molecular weight greater than 150, generally have N.O.E. values approaching the maximum; also in large rigid molecules, non proton bearing carbons have been observed to give the full N.O.E.

There are two reasons why integration of the peak areas of signals in decoupled spectra do not correspond to the numbers of nuclei giving rise to the signal. One is that the N.O.E. varies for different nuclei in a sample and for carbon nuclei is dependent on the importance of dipole-dipole relaxation in the overall relaxation of the nucleus.

The second reason concerns the different rates of spin lattice relaxation of the various atoms in a sample. In an F.T. experiment the pulse repetition rate is of the order of 0.1 to 1 sec whereas the spin-lattice relaxation time of most organic compounds is 1 to 20 sec and it takes about five times the spin lattice relaxation time to restore the nuclear spin state populations to their thermal equilibrium value. Thus nuclei with long T_1 times will not have sufficient time to fully relax between successive pulses. The signal from partially relaxed nuclei is not as intense as that from a fully relaxed system, since the signal intensity is proportional to the number of excess nuclei in the lower energy level.

If a nucleus has an exceptionally long relaxation time then its signal may be too low in intensity to be visible in the spectrum. In such cases it is advantageous to add a paramagnetic material to the sample. The magnetic moment of the unpaired electron is about 700 times that of a proton; thus all the nuclei in the sample relax much more efficiently as a result of dipole-dipole interactions of the nuclei with the electron, and this process will dominate the total relaxation of the sample. A common paramagnetic reagent is $Cr(acac)_3$, and this was claimed not to change the chemical shifts of the nuclei[7], a view which has recently been challenged.[8]

METHODS OF DECOUPLING.

Ernst[9] developed a practical way to achieve complete proton decoupling in ^{13}C spectra by using a single proton decoupling frequency as the centre of a finite excitation band. The single frequency was modulated by a pseudo random noise generator yielding effective excitation throughout a preset bandwidth, corresponding to sequential irradiation of all proton frequencies within the time necessary to observe all the carbon resonances. A 10 fold enhancement for the pulse technique over the c.w. method is obtained from the collapse of the multiplets and Overhauser enhancement.

Wide band decoupling results in the loss of all spin-spin coupling information. A technique called single

frequency off-resonance decoupling, which allows the retention of direct carbon hydrogen spin-spin coupling data but removes all long range carbon hydrogen spin-spin coupling, is achieved by maintaining proton irradiation at high power levels but the centre frequency is moved 500 - 1000 Hz distant from the proton frequencies which are to be irradiated. The excitation bandwidth generator is not used in this type of decoupling.

Off-resonance decoupling yields the following information which is very useful in assigning ^{13}C spectra. Non proton bearing carbons, methine, methylene and methyl carbons appear respectively as singlets, doublets, triplets and quartets in the off-resonance spectrum.

The spin-spin coupling between carbon and hydrogen, J_{C-H}, observed in the off resonance experiment is not the true J_{C-H} but the residual coupling, J_R, and is given by the formula:-

$$J_R = \frac{J_{C-H} \times \delta_z}{\frac{\gamma H_2}{2\pi}}$$

where J_R = the observed spin-spin coupling

J_{C-H} = the true spin-spin coupling

δ_z = The number of Hertz the centre frequency of the source of proton irradiation is distant from the signal being decoupled

$\frac{\gamma H_2}{2\pi}$ = the radio frequency power of decoupling

The usual type of decoupling employed in proton spectra, proton homonuclear decoupling, is occasionally useful in assigning ^{13}C spectra. If from proton spectra the resonance frequencies of protons coupled to specific carbons can be recognised, then these protons are irradiated at low power in ^{13}C experiment, resulting in the collapse of the signal for the carbon bearing protons to a singlet, whereas others remain as multiplets.

THE THEORY OF THE CHEMICAL SHIFT[10]

For a given nucleus A the magnetic field H_A required to bring about the resonance condition at a particular irradiating frequency, H_0, is given by:

$$H_A = H_0 \quad (1 - \sigma_A)$$

where σ_A is the screening or shielding constant and is a function of the chemical environment of the nucleus.

Most attempts to calculate the value of this shielding constant on theoretical grounds are based on the Ramsey equation[11] which was developed from second order perturbation theory. This equation represents the difference between two terms of comparable magnitude; one of these terms requires detailed knowledge of the energies and wave functions of all the excited states including those in the continuum, thus its practical use especially for large molecules is limited.

A simplification suggested by Saika and Schlichter[12] involves the partition of σ_A into several components thus:

$$\sigma_A = \sigma^{AA}_{dia} + \sigma^{AA}_{para} + \sum_{B \neq A} \sigma^{BA}$$

Pople[13] further portioned the third term in the above expression into separate inter and intra atomic terms:

$$\sigma_A = \sigma^{AA}_{dia} + \sigma^{AA}_{para} + \sum_{B \neq A} \sigma^{BA} + \sigma^{A}_{deloc} + \sigma^{A}_{solv}$$

The first three terms represent intra atomic terms, the fourth represents inter atomic terms.

σ^{AA}_{dia}, the diamagnetic shielding term, is associated with the electrons moving freely round the nucleus in a spherically symmetrical s state and represents the diamagnetic Lamb term[14] which is derived from Ramsey's formula:

$$\sigma^{AA}_{dia} = \frac{e^2}{3mc^2} \sum_i \left\langle r_i^{-1} \right\rangle$$

$\left\langle r_i^{-1} \right\rangle$ is the mean inverse distance of electron i from the nucleus of interest.

σ^{AA}_{para}, the paramagnetic shielding term, is a local corrective term which takes into account the non spherical electronic nature of the atom, resulting from the mixing of ground and excited states by the applied field (n, p electronic states).

$\sum_{B \neq A} \sigma^{BA}$ represents a summation of contributions to A from intra atomic current induced in all atoms B ≠ A and is related to their magnetic anisotropy.

σ^{A}_{deloc} is an inter atomic contribution which applies to cyclic systems. This contribution arises from the current produced by electrons which are delocalised in the ring of the molecule i.e. the 'ring current'.

σ_{solv} represents the contributions of the solvent to the screening of A.

Such a calculation obviously involves a significant error and the absolute screening constant cannot be calculated. However, differential shieldings may be assessed and the smaller the number of contributions involved, the more accurate the computation.

The dominant term in the above expression as applied to carbon screening is σ^{AA}_{para}. Karplus and Pople[15] derived the following expression for σ^{AA}_{para}

$$\sigma^{AA}_{para} = \frac{-e^2 \hbar^2}{2m^2c^2} (\Delta E)^{-1} \left\langle \frac{1}{r^3} \right\rangle_{2p} \left[q_{AA} + \sum_{B \neq A} q_{AB} \right]$$

Several expressions were derived for σ^{AA}_{para}; the one above is the most practical and it contains several simplifications.

$\frac{-e^2 \hbar^2}{2m^2c^2}$ is a constant and the negative sign corresponds to the paramagnetic effect.

$\left\langle \frac{1}{r^3} \right\rangle_{2p}$ is the mean value of $\frac{1}{r^3}$ where r is the distance between the nucleus and the 2p electrons. An electron withdrawing group shortens the distance between the nucleus

and the 2p electrons. This increases the negative value of σ^{AA}_{para} causing a paramagnetic shift.

(ΔE) is the mean excitation energy and is a semi-empirical term which is substituted for $(E_j - E_i)$ in the full expression.

$(E_j - E_i)$ is related to the excitation energy of the molecule associated with the m.o. transition of electrons in the occupied orbital i to the unoccupied orbital j. Many attempts have been made to calculate a value for ΔE. Pople[16] considers that for an Sp^3 hybridised alkane carbon value, 10 e.V. is a good approximation.

The electronic transitions $n \rightarrow \pi^*$, $\sigma \rightarrow \sigma^*$ and $\sigma \rightarrow \pi^*$ are related to ΔE, thus electronic and photo-electronic spectra offer in principle a means of estimating the mean excitation energy. Mason[17] has shown that ΔE decreases as λ max. increases in the series.

CH_4 (140 nm) ; C_2H_6 (150 nm) ; C_3H_8 (156 nm) ; C_4H_{10} (163 nm).

Since σ^{AA}_{para} is a function of ΔE, a paramagnetic shift of the ^{13}C chemical shift arises from a decrease in the ΔE value and the low field resonance observed in unsaturated compounds with respect to alkanes can be rationalised on this basis.

	Alkanes	Alkenes	Ketones
ΔE (in e.V.)	10	8	7

σ^{AA}_{dia} is generally considered to contribute less than 10 per cent to the total screening[18].

The calculation of the diamagnetic screening constant presented certain difficulties as it required a knowledge of molecular electronic wavefunctions. However, Flygare and Goodisman[19] calculated an all atom value for σ_d by the contributions of all atoms in the molecule to the free atom shielding. However, the all atom σ_d increases monotonically with the number of electrons in the molecule and can become very large, for example, with increase in alkyl substituents.

In order to obtain a truer measure of σ_d, Mason[17] proposed the use of a local σ_d, obtained by summation over only the atom in question and those bonded directly to it.

With this method Mason has been able to explain the relative decrease of the paramagnetic shift of the carbon atom resonances in chloromethanes due to increasing halogen substitution. Mason's proposal to include only a diamagnetic contribution from the atom in question and atoms α to it, has been criticised as leading to artificially large values for the diamagnetic contribution and thus to important substituent effects. Lippmaa[20] argues that there is no reason to include only α effects and the inclusion of a β contribution would make the calculated diamagnetic contribution too high. Witanowski[21] calculates that the diamagnetic contributions to the ^{15}N chemical shifts obtained by this method are of an order of magnitude larger and of opposite sign from the values expected.

A great deal of work has been devoted to the magnetic anisotropy contribution $\sum_{B \neq A} \sigma^{BA}$ of the proton chemical shift. As this term depends only on the nature of the neighbouring atoms, the results of the proton spectroscopy should be applicable to other nuclei. The anisotropy contribution is usually only a few per cent of the total screening constant for carbon and it is usually ignored.

When the shielding arises from bonds of axial symmetry (single and triple bonds) the paramagnetic contribution of neighbouring atoms[16] may be written as :

$$\sum_{B \neq A} \sigma^{BA} = \frac{-1}{3N} \sum_{B \neq A} \Delta\chi^{B} \frac{(1 - 3\cos^2\theta)}{R^3_B}$$

$$\Delta\chi^{B} = \chi^{B}_{\parallel} - \chi^{B}_{\perp}$$

where N is Avogadros number

$\chi^{B}_{\parallel}$ and $\chi^{B}_{\perp}$ are the components of magnetic susceptibility tensor which are parallel and normal to the direction of symmetry axis.

R_B is the distance A B

θ is the angle BA makes with the symmetry axis

The expression is, however, only approximate[22] as the shape of the electronic distribution is not taken into account and σ^{BA} represents a long range shielding.

Anisotropy has frequently been invoked to explain discrepancies between observed and calculated chemical shift values. The deviation of heavy halogen substituents from a correlation of the ^{1}H and ^{13}C chemical shifts of substituted methanes and ethanes with substituent electronegativity are attributed to this effect.[23] These ideas were extensively adopted in much of the ^{13}C shift work that was reported during the early and mid 1960's.

Cheney and Grant[24] argued that the neighbour anisotropy effect could not account for such large contributions to ^{13}C chemical shifts. Since the effect is dependent only on the geometrical relationship of the nucleus and the magnetically anisotropic group, and is essentially independent of the nucleus, there is no reason to expect that neighbour anisotropy effects on ^{13}C shieldings should be an order of magnitude greater than for ^{1}H. Thus in the case of atoms that are not directly bonded to the substituent, deviations from the correlations of ^{13}C shifts with substituent electronegativity are not attributable to the neighbour anisotropy effect.

Many theories have been postulated to explain the anomalous influence of the heavy halogens on ^{13}C chemical shifts. Schaefer et al[25] rationalised the effect in ethyl halides by invoking intramolecular dispersion forces exerted by the halogen on the methyl carbon. This intramolecular field effect was postulated by analogy with the intermolecular dispersion effect found in halogenated solvents. Litchmann and Grant[26] proposed that the large increase in carbon shielding on substituting methane with iodine was primarily of steric origin; another possibility is that the increase is due to high ionic character in the C - I bond.[27]

In heavy atoms such as iodine, a 'spin polarisation' shift (L S shift)[28,29] caused by large spin orbit coupling interactions could be responsible for the substituent effects shown by this atom. The interaction is caused by coupling of the external field with the electron orbit, L, and the electron spin, S, the latter term also coupling with the nuclear spin, I. The spin polarisation

chemical shift is possibly propagated by a mechanism similar to that of spin polarisation in spin-spin coupling. If this is the case, it is expected that the 'spin polarisation' effect should exhibit a marked conformational dependence.

σ^{A}_{deloc} is an inter atomic term and has been shown by Pople[30] to be associated with the ring current effect. The effect has been demonstrated in non alternant hydrocarbons such as bridged annulenes[31], where the bridged carbon atoms are strongly shielded.

In saturated systems the ring current effect has been used to explain the difference in chemical shift between cyclopropane and other cyclic hydrocarbons.[32,33] As in the case of anisotropy the ring current effect is geometry dependent and can yield useful stereochemical information, such as that used by Dhami and Stothers[34] in their study of acetophenones and styrenes.

PARAMETERS REPRESENTATIVE OF THE ELECTRONIC PROPERTIES OF SUBSTITUENTS.

There are three main methods of estimating the electronic properties of substituents. They are :-

(1) Group Electronegativity
(2) Hammett constants
(3) Molecular orbital calculations.

Each of these finds important application in rationalising substituent effects in n.m.r. spectroscopy and are discussed in detail below.

GROUP ELECTRONEGATIVITY[35]

The term electronegativity was introduced by Pauling[36] to describe the ability of an atom in a molecule to attract electrons to itself. It rapidly became a widely used concept and considerable effort has been expended in attempts to derive a universal quantitative set of electronegativity values.

In the approximation that permits polyatomic groups to be regarded as pseudo-atoms, the corresponding group electronegativities may be considered.

With the increasing amount of n.m.r. data available during the mid 1950's, several attempts were made to construct an electronegativity scale using proton n.m.r. chemical shifts.

Allred and Rochow[37] reported that the relative proton chemical shifts of methyl halides in infinitely dilute carbon tetrachloride solution are linearly related to halogen electronegativities obtained from other methods. However, for other methyl derivatives this relationship is not valid.

The paramagnetic contribution to the total shielding of protons is considered to be zero and the contribution from all other atoms should remain constant for a given C - H bond. In molecules of the type $R - \overset{H_\alpha}{\underset{H_\alpha}{C}} - X$, the proton chemical shifts of H_α for different substituents (X) measure the change in ionic character of the C - H bond and the relative electron withdrawing character of each substituent group. The change in chemical shift is

due mainly to the diamagnetic term which arises from the effect of bonding electrons on the population of an atomic 1s orbital centred on a given hydrogen atom.

Dailey and Schoolery[38] considered that the internal chemical shift difference between the chemical shifts of methyl and methylene protons in substituted ethyl derivatives would give a measure of substituent electronegativity. However, deviations between the electronegativity values, E_R, calculated by this method and electronegativities derived from vibrational and thermodynamic data, attributed to magnetic anisotropy effects, are found in order NO_2, I > Br > Cl > SR.

Cavanaugh and Dailey[39] revised the values of Dailey and Schoolery[38] as the latter were determined in benzene solution which was subsequently found to give rise to anomalous dilution effects.

They give no value for the nitro group, since it is considered that the double bond character of the C - N bond in nitro derivatives, makes it sufficiently different in nature from other substituents not to be directly comparable to them. It is also calculated that anisotropy effects in methyl halides are not as great as was first assumed.

The electronegativity values used by us are given in Table(1).

HAMMETT CONSTANTS[40]

The Hammett equation is a linear free energy relationship and is usually expressed[41,42] in the form

$$\log k = \log k^{o} + \rho\sigma$$

where k denotes the rate of a given reaction for a substituted compound.

k^{o} denotes the rate of reaction for the unsubstituted compound.

σ is a characteristic of the substituent and is independent of the reaction type.

ρ is determined by the nature of the reaction and the reaction conditions.

The equation was originally used for reactions on the side chains of benzene rings for which the substituent

was meta or para, where the σ constants are denoted by σ_M and σ_p respectively.

Hammett[41] introduced the standard that the value of ρ for the dissociation of benzoic acids in water at 25°C is taken as unity. Thus the values of σ_p and σ_M are the experimental substituent effects and are called primary σ values.

Many estimates of these values have been made and, since most determinations are made in aqueous or aqueous alcoholic solutions, it is difficult to remove all substituent - solvent interactions[42], especially when the substituent can hydrogen bond i.e. hydroxyl and amino.

It should be noted that the σ constant expresses only the influence of the substituent on the rest of the molecule and not its intrinsic properties. As primary steric effects are excluded by virtue of the geometry of the aromatic system, electronic effects are most important and it was recognised that these can be understood in terms of a combination inductive, I, and mesomeric, M, effects.

The I effect includes contributions from field effects and polarisation of σ and π bonds whereas the M effect is taken to include all effects which differ when the group is in meta or para position e.g. conjugation. Many attempts have been made to quantify the importance of I and M effects in the various Hammett constants.

As a first approximation, σ_p was assumed to be a mixture of I and M effects whereas σ_M measured the inductive effect and their difference was taken as a measure of the M effect.[43]

A more quantitative approach to this problem was utilised by Taft et al.[44] The relative I effects of substituents were determined by use of rigid cyclic systems, where there could be no direct mesomeric interaction between the substituent and the reaction centre. The dissociation constants of 4 - substituted bicyclo [2.2.2.] octane - 1 - carboxylic acids[45] or α - substituted toluic acids[43] are used as the I scale, σ_I.

Taft[44] assumed that the σ_I values from bicyclo [2.2.2.] octane derivatives and σ_M and σ_p values from benzene derivatives were on a common scale, because of the similarities

in the systems and he calculated mesomeric constants, σ_R, from the equation;

$$\sigma_P = \sigma_I + \sigma_R$$

From the scale of values obtained for σ_R, σ_M, can be expressed thus

$$\sigma_M = \sigma_I + \alpha \sigma_R$$

where α was found experimentally to be 0.33.

In the equations above, it was assumed that the inductive effect at the meta and para positions is identical. However, the inductive effect of a substituent, as monitored, for example, by the dissociation of meta and para-nitrobenzoic acids[43], is more strongly felt at the para position. Thus a general expression for the σ constants is given by

$$\sigma = \lambda \sigma_I + \alpha \sigma_R$$

where for σ_p : $\lambda = 1.14$, $\alpha = 1$

for σ_M : $\lambda = 1$, $\alpha = 0.33$

The main success of this treatment was to provide a general scale for the inductive effect. The relative contributions of I and M effects to σ constants from various sources could also be obtained by this method. However, the values of σ_R derived from σ_P tend to be small especially for mesomerically electron withdrawing substituents, for example, NO_2, CF_3, CN are all zero on this scale. Very little improvement is obtained if σ_{p^o} [44,46] is used instead of σ_p. σ^o values are derived from the dissociation of phenylacetic acids, where mesomeric donors such as NH_2 cannot enter into direct conjugation with the carboxyl group as in the benzoic acid case.

Taft et al[47] considers that there is no universal σ_R scale and four different scales are necessary to define the resonance contribution which arises in different situations. These are as follows:-

σ_R^o for weak π donors such as halogens.

σ_R (BA) for weak to moderate π acceptor groups such as benzoic acids.

σ_R^+ for situations in which the system carries a net positive charge.

σ_R^- for situations in which the system carries a net negative charge.

The use of single reactivity parameters, such as σ_p or σ_M, in correlating substituent effects is limited, since each parameter is a mixture of an I effect and an M effect and linear relationships with substituents are obtained only when the I/M ratio is the same in the observed effect and the reactivity parameter.

A more general method is to use a Dual Substituent Parameter (D.S.P.) treatment of experimental results involving combinations of σ_I, to measure the inductive effect, and the appropriate σ_R value as described above. These are used in an equation of the type[47] :-

$$\Delta = \rho_I \sigma_I + \rho_R \sigma_R$$

where Δ is the experimental substituent effect.

ρ_I, ρ_R, are the weightings of σ_I and σ_R.

A second approach is that of Swain and Lupton[48] which uses the same σ_I values as Taft[47], which they denote as F, a field effect including through space field effects and through the bonds inductive effects as one parameter.

To obtain their resonance scale, R, they assume that the R value of $\overset{+}{N}Me_3$ is zero and then calculate the value of R for the other substituents from the equation

$$\sigma_p = \alpha F + R$$

where α = 0.56 as R = 0 for $\overset{+}{N}Me_3$

The two scales F and R can be used to correlate substituent effects (Δ), as before, in the equation

$$\Delta = f F + r R$$

where f, r are the weightings factors of F and R.
The percentage resonance effect is given by

$$\% R = \frac{100 \Psi |r|}{\phi |f| + \Psi |r|}$$

where ϕ = 0.365 , Ψ = 0.228

The constants ϕ, Ψ were introduced by Swain and Lupton to compensate for the fact that the average variation of each F value from their mean value, is greater than the

than the average variation of each R value from their mean value.

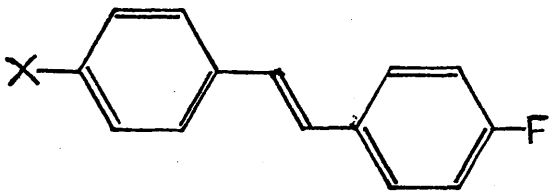
Phillips et al[49,50] use the following equation in their study of substituent effects on ^{19}F chemical shifts in aromatic systems,

$$\Delta = f' F + r' \sigma_p$$

where f' and r' are weighting factors.

In this formalism F represents effects transmitted through space and through the σ bonded framework whereas σ_p is claimed to measure those effects transmitted through the π system.

The evidence for this is that the substituent effects on the ^{19}F chemical shifts of 4 - X, 4' - F substituted trans-stilbenes (2) correlates with σ_p



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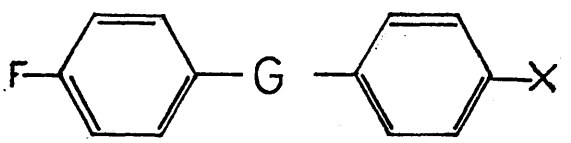


(3)

and since eleven bonds separate the fluorine atom from the substituent, inductive effects should be negligible, the substituent effects should be completely transmitted via the π system, hence σ_p is the best measure of effects transmitted in this manner.

The use of the D.S.P. approach to rationalise substituent effects has been the subject of much controversy in the literature. Exner[43] criticises the Swain and Lupton[48] approach as it assumes a general resonance scale for all situations and the standard deviations obtained in correlations between the σ_p^+ and σ_p^- scale with F and R are too large.

Wiley and Miller's[51] criticism of the Swain and Lupton[48] approach has been discussed by Reynolds[52] and he indicates several flaws in Wiley and Miller's[51] objections.

Phillips[50] points out that in the Taft[47] D.S.P. treatment there are seven variables σ_I, ρ_I, ρ_R and four σ_R values. Utilising this number of degrees of freedom should allow correlation of any substituent effect, with

high correlation coefficient and he further claims that spurious mechanisms of electronic effects could be arrived at by this method.

In an investigation of ^{19}F chemical shifts of molecules of the type (3) where the cavity, G, represents a series of linking groups for example -N = N-, $-CH_2-$, Tafts group[53] show that solvent effects cause a variation in value of λ, σ_R/σ_I. They claim that the magnitude of σ_I is more sensitive to solvent effects than the magnitude of σ_R. They also conclude that Phillips[49] correlation of the ^{19}F chemical shifts in (3) is fortuitous and would not be valid on change of solvent. It is also claimed that the correlation is not valid because it shows slight curvature which is said to become linear on correlation with σ_I and σ_R. The values of Hammett constants used in this thesis are given in Table (1).

MOLECULAR ORBITAL CALCULATIONS[55,56,57]

There are various levels of all valence electron semi empirical molecular orbital methods, which use a basic Self Consistent Field, (S.C.F.) approach but which differ in the methods used to obtain values for the large number of integrals which cannot be quantitatively evaluated.

The normal process is to calculate the total energy of the system by an iterative method involving approximate expressions for the relevant wave functions and Hamiltonian operators, until the total energy converges to a minimum on successive iteration.

This procedure generates a density matrix from which bond orders and charge densities may be extracted.

In a priori M.O. methods all integrals are evaluated rigorously by substituting complex functions for each atomic orbital in the total wave function. For molecules containing more than two atoms, this process becomes impractical even with the most sophisticated computers. In order to conduct M.O. calculations on more complex molecules, certain approximations must be made to reduce the amount of computation.

In the lower level methods, C.N.D.O. and I.N.D.O., interaction between outer electrons and the atomic core, and the less important integrals, are ignored, while those

which are important but which cannot be accurately calculated, are estimated by empirical parameterisation.

Differential overlap is the product of the wave functions of two atomic orbitals. In the zero differential overlap approximation, differential overlap between any pair of orbitals on the same centre is zero. Each atom or centre contributes several orbitals to the system. This approximation is the basis of the Complete Neglect of Differential Overlap (C.N.D.O.) method.[57]

The various Hamiltonian operators involved in the calculations are estimated by parameterisation, that is, by substituting experimental data into an expression for the Hamiltonian. In the C.N.D.O./2 method[57] the average of the ionisation potential and the electron affinities are used to approximate the Hamiltonian of an atom.

The wave functions are constructed from Slater Type Orbitals (S.T.O.) and these functions are used in the iterative process described previously.

Pople and Segal's[57] C.N.D.O./2 method has been successful in predicting bond angles, dipole moments, bending force constants, bond lengths and n.m.r. chemical shift trends.

This is the simplest of Pople's semi empirical methods, the next level of approximation Intermediate Neglect of Differential Overlap (I.N.D.O.)[58] does not neglect the one centre integrals, i.e. differential overlap between orbitals on the atom. I.N.D.O. also takes into account that electrons can have parallel or anti-parallel spins; hence this method was used to calculate spin densities and hyperfine coupling constants.

The highest level of semi-empirical theory is ab initio theory[59] where 1s electrons are included in this method as part of an unpolarisable core. This method uses gaussian orbitals, which are different from those used in lower level methods. Gaussian orbitals allow quicker evaluation of two electron integrals which are neglected or parameterised in more approximate methods.

The calculation of electronic populations by the C.N.D.O./2[57] method takes much less time than using ab initio theory.[59] The charge distributions obtained by the

C.N.D.O./2 method parallel those calculated by the ab initio method, which is considered to be the most accurate method currently in use. However, the energies obtained by the former method are not reliable owing to the approximations used.

Pople carried out his C.N.D.O./2 calculations in order to examine the charge densities in simple molecules. The results[60] were surprising in that the distributions of charge which were calculated by this method were not consistent with the nature of the inductive effect as it was understood at the time. For example, the common interpretation of fluorine is that it is an inductive type substituent leading to positive character in a saturated hydrocarbon

$$\overset{\delta-}{F} - \overset{\delta+}{C} - \overset{\delta++}{C} - \overset{\delta+++}{C} \qquad (4)$$

$$\overset{\delta-}{F} - \overset{\delta+}{C} - \overset{\delta--}{C} - \overset{\delta++}{C} \qquad (5)$$

which diminishes steadily with distance down the chain as in (4).

The calculations rather suggest that the induced charges alternate in a decaying manner so that the β position is normally negative as in (5).

There is no strong evidence to support this postulate although the existence of alternation has been invoked to explain certain aspects of n.m.r. spectra.

The calculations are carried out on a C.N.D.O. - I.N.D.O. program[54] which can accommodate up to 30 atoms, or 70 basis functions, which ever is the smaller number.

The program is capable of performing I.N.D.O. calculations on the elements hydrogen to fluorine while it can carry out C.N.D.O./2 calculations on both first and second row elements.

In order to operate the program, the following information is required; the co-ordinates of each atom, given in angstroms (in cartesian form), the atomic number of each element, and the net charge on molecule.

Bond lengths and angles are normally taken from a table of standard (S.T.D.) bondlengths and angles,[54,60] however in certain cases the co-ordinate system can be taken directly

from an X-ray structure of the molecule, if this is available.

The output from the program lists the atomic charge of each atom plus the total energy and dipole moment of the molecule. From information in the density matrix the atomic charge on an atom may be dissected into the various constituent contributions from each orbital. This matrix also contains the electronic population between any two atoms in the molecule, the bond order.

THE CARBON-13 CHEMICAL SHIFTS OF ORGANIC MOLECULES.

1) Aliphatic systems.

A) Unsubstituted alkanes and the representation of carbon-13 chemical shifts by substituent parameters.

Grant and Paul[61] have published one of the most detailed studies on linear and branched alkanes, of chain length up to ten carbon atoms. The results show that the carbon atom of methane experiences a progressive downfield shift on successive substitution by methyl groups. This low field shift is general for most classes of compound.

It is also found that the substitution of a β-hydrogen by a methyl group causes a deshielding effect in the carbon atom, which is one atom removed from the point of substitution.

The γ-effect is, generally, a shielding effect and is thought to be mainly due to a through space interaction although its exact nature is not understood.

The consistent shift trends that were found on the homologation of alkanes led Grant and Paul to construct an incremental system in order to predict the chemical shifts in linear alkanes. Their parameters can predict chemical shifts of linear alkanes to an accuracy of 0.21 p.p.m. These parameters fail in the case of branched alkanes where additional parameters are required in order to adequately account for particular branching situations.

Alternatively, Savitsky and Namikawa[62] investigated the possibility of an additive relationship for predicting chemical shifts using carbon shieldings. For saturated systems a series of five factors for the bonds directly involved were calculated by least squares analysis of a wide ranging series of unsubstituted hydrocarbons. The factors used were H-, $-CH_3-$, $-CH_2-$, $-\overset{|}{C}H-$ and $-\overset{|}{\underset{|}{C}}-$. The inclusion of an additional factor for the γ-effect enabled the authors to predict the chemical shifts of acyclic alkanes to within 2 p.p.m.

The chemical shifts of cycloalkanes from cyclobutane to cycloheptadecane occur in the range 23 - 29 p.p.m.[63] and for rings containing more than fourteen carbon atoms the chemical shift value is fairly constant. In these systems

there is no correlation between ^{13}C chemical shifts and the corresponding proton chemical shift.

In cyclopropane[63] the carbon and hydrogen atoms both absorb at a relatively high field. It is calculated that a ring current would explain the high field shielding involved in these shifts although there is no theoretical justification for assuming that one exists in cyclopropane.

The additivity parameters of Savitsky and Namikawa[62] fail to predict the chemical shifts of polycyclic aliphatic systems even if they are strain free as in adamantane.[64] Lippmaa's group[65] have suggested that a diamagnetic correction of 6 p.p.m. should be included for every 5 or 6 membered ring connected to the carbon in question. While this certainly improves the value of the predicted chemical shifts, lack of sufficient data prevents further investigation into the validity of the term.

Methyl substituent parameters which have been calculated for methyl substituted cyclohexanes[66] can predict the chemical shifts of the ring carbons of these systems to within 0.51 p.p.m. They can also rationalise the methyl chemical shifts in terms of steric crowding and conformational effects.

B) The Chemical shifts of substituted aliphatic systems.

i) Acyclic systems.

In one of the first studies of substituted aliphatic systems Lauterbur[67] measured the chemical shifts of a number of alkyl derivatives. A moderate correlation was obtained between the chemical shifts of mono substituted methyl halides with the Pauling electronegativity[36] of the substituent.

The chemical shifts of each series of chloro, bromo, iodo or methoxy substituted methanes increases smoothly although not linearly[67] with increasing substitution and they pass through a common point corresponding to methane. Additive shift changes were produced by the interchange of halogens in polyhalogenomethanes.

The chemical shifts of halogenomethanes have been redetermined[26] recently and it was found that, although no simple additive relationship can adequately account for the

chemical shifts in these compounds, a statistical approach which includes a "pair interaction term" to account for the combined effect of two halogens bonded to a single carbon can reproduce the ^{13}C chemical shifts of halogenomethanes with a fair degree of accuracy.

In their study of mono-substituted methyl and ethyl derivatives, Spiescke and Schneider[23] employed an approach to analyse the shift values which was widely used throughout the 1960's. They demonstrated that, if a correction was made for the neighbour anisotropy of a substituent, then a correlation could be obtained between ^{13}C chemical shifts and electronegativity for all common substituents.

Savitsky and Namikawa[68] in an investigation of the additivity of the chemical shifts of the series $(CH_3)_n$-CH_{3-n}-X computed a quantity, Δx, from the average of three α-chemical shift differences (δ Me - δ Et), (δ Et - δ iPr), (δ iPr - δ tBu) for each substituent. Δx was found to increase linearly with the increase in the C - X bond length. This suggested that the α chemical shifts in these systems are related to the relative polarisability of the electron density in the C - X bond by the inductive effect. The shift of electron density away from the α carbon towards the electronegative group X due to the electropositive inductive effect of an additional methyl group is more important in a longer than a shorter C - X bond.

A comparison of the shieldings of cyclic and acyclic alcohols[69] with the corresponding alkanes shows that the α- and γ-effects of the alcohols are greater than for the corresponding alkanes. The position of the hydroxyl group on the alkyl chain of acyclic alcohols greatly affects the magnitude of the α-effect and branching decreases its value significantly. This it was suggested is due to variations in the polarisability of the hydroxyl group.

Hagen and Roberts[70] have studied the shieldings of lower aliphatic carboxylic acids and their anions. They find that the α-carbons of the anions are more deshielded than in the acids themselves which is surprising as the acid anion is less electronegative than the acid. It is also found that the rate of attenuation of the difference

($\delta C^{RCOO^-} - \delta C^{R-COOH}$) along a given alkyl chain is close to that expected for an r^{-3} dependence in the situation where the negative charge is centred between the oxygens of the carboxyl group and the alkyl chain is in the extended staggered conformation. This is similar to the result found for proton shieldings in the aliphatic chain of the anions and acids.[71] It has been suggested that this result is evidence of a "through-space" effect as it is linked with the anisotropy of the carboxylate group. Horsely and Sternlicht[72] consider that these changes arise from a C - H bond polarisation caused by the negatively charged carboxylate anion.

ii) Alicyclic Systems.

The chemical shifts of substituted cyclopropanes have been reported by several groups.[73-75] The α effects of mono-substituted cyclopropanes[73] are roughly similar to those of methane, the deviations have been rationalised in terms of the different electronic and geometrical relationship between the substituent and hydrocarbon in the two systems. No relationship between α and β carbon shifts in cyclopropanes has been reported but it has been noted that substituents which cause an increase in J_{C-H} also cause an increase in J_{C-H}.

Lippmaa et al[76] have reported the chemical shifts of 36 monosubstituted cyclohexanes. Here the chemical shifts of α and β carbons correlate linearly with the methine and methyl carbons, respectively, of similarly substituted isopropyl groups. This result is surprising in that the substituted cyclohexanes are statistical means of axially and equatorially substituted carbon atoms and the amounts of axial vs equatorial character will vary with the nature of the substituent.

The γ effect in n-amyl derivatives is more shielding than that found for the cyclohexyl derivatives, which is surprising since larger non bonded interactions are expected in the latter case. However, the γ effects of substituted octanes containing a CHX grouping and two γ interactions, as in cyclohexane, are 1.6 times smaller than for 1-substituted octanes.[77]

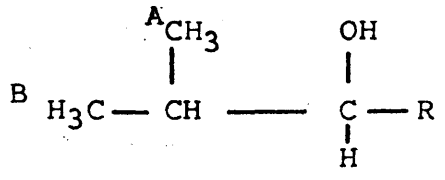
The δ-shifts of cyclohexanes[76] are to high field whereas those in a comparable aliphatic series, n-pentanes, vary little with change of substituent. It is concluded that there must be a difference in the mechanism of the δ-effect in the two systems.

Since equatorial substituents, which have a small steric effect on the δ-carbon, produce the largest δ-effects, the δ-effect is attributed to a through-the-bonds inductive effect and a fair correlation is obtained between the δ-chemical shifts and inductive parameter, σ^*, after a correction is applied to the shifts of the halogen derivatives.

In order to explain these high field shifts Lippmaa's group relate the magnitudes of the chemical shifts to the charges on the carbon atoms and postulate that there are more favourable conditions for charge delocalisation in alicyclic derivatives than in their acyclic counterparts. In support of this proposition, they cite the evidence for charge alternation found in cyclohexanes[78], in chloroadamantane[79], in simple aliphatics[80] and the work of Pople's group.[60]

There is one anomoly in this argument in that the δ carbons in, for example, the-CH_2 OH and -OH derivatives should have opposite signs, and to comply with the rationalisation above, the charges would have to conform to the classical inductive effect, a monotonous attenuating variation in charge, in an external chain, which becomes an alternating attenuating variation in charge in a ring system. This proposition is in conflict with Pople's calculations on the alternation effect which indicate charge alternation in both cyclic and acyclic systems.

The 1, 4 gauche interaction is known to cause upfield shifts by steric interactions, the steric 1, 5 interaction is found to cause downfield shifts.[81] In the molecule (6) when



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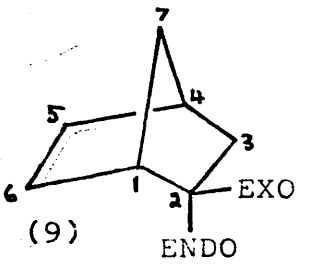


(9)

R is a methyl group the chemical shift difference $\delta_A - \delta_B$ is small and is due to a 1, 4 methyl-methyl and a 1, 4 methyl-hydroxyl interaction. When R is changed to an ethyl group the usual steric arguments fail to explain the large shifts involved and a 1, 5 methyl-methyl interaction producing a downfield shift needs to be invoked.

A comparison of the methyl shieldings for cis 3,3,5 - trimethylcyclohexanol (7) and 3,3,5,5 - tetramethylcyclohexanol (8)[82] indicates that the single axial methyl group in (7) absorbs at 25.6 p.p.m. while the two axial methyl groups in (8) resonate at 27.7 p.p.m. suggesting that a <u>syn</u> axial 1, 5 dimethyl interaction causes a downfield shift.

A second order field effect has been calculated to be of suitable magnitude to cause these shift differences.[83]

iii) Polycyclic Systems.

The α and β effects of 2- substituted norbornanes[84] are only affected by the orientation of the substituent to a minor degree; <u>endo</u> shifts are consistently smaller than <u>exo</u> shifts by <u>ca</u> 1 - 2 p.p.m. This is due to either electronic effects or ring distortion in the <u>endo</u> series. α and β effects in these systems are smaller than those found in acyclic systems and the β effect in norbornanes is different at $C_{(1)}$ and $C_{(3)}$, decreasing for different types of carbon atom in the order secondary > tertiary > quaternary.

It is suggested that α and β effects in ^{13}C n.m.r. are mutually dependent on the degree of substitution at both positions and this reflects the replacement of hydrogen, rather than the nature of the incoming group. The replacement of a hydrogen in the α or β position decreases the magnitude of both the α and β shift by approximately 3 p.p.m.

From these observations it is concluded that the substituent parameters consist of a fundamental value which is inductive in origin plus a variable term which depends on the number of substituents at the α and β positions. Also β shifts tend to reach a limiting value in highly

substituted systems.

A possible mechanism to account for these factors proposed that the variable term is dependent on the perturbation of the C_{α} - C_{β} bond which causes an upfield shift. Thus this effect is independent of the site of substitution and since the distortion of the C_{α} - C_{β} bond is limited, causing the β effect to reach a maximum value, the α effect will be more influenced by the polarisation of the C_{α} - X bond and has more sensitivity to the variation of substituent. The smaller α and β effects of <u>endo</u> relative to <u>exo</u> substituents are rationalised in terms of the greater steric interactions in the former causing larger perturbation of the C_{α} - C_{β} bond and hence an upfield shift.

In norbornane three carbons, $C_{(4)}$, $C_{(6)}$ and $C_{(7)}$ are γ to $C_{(2)}$. The γ shifts of $C_{(4)}$ are small owing to its distance from $C_{(2)}$ and while <u>endo</u> - 2 - substituents slightly deshield $C_{(7)}$, <u>exo</u> - 2 - substituents shield this nucleus. $C_{(6)}$ is invariably shielded by both substituent orientations although the shielding is slightly less for <u>exo</u> substituents.

The degree of shielding of $C_{(6)}$ by an <u>endo</u> $C_{(2)}$ substituent is crudely related to the size of the substituent but clearly the shielding of $C_{(6)}$ by an <u>exo</u> - $C_{(2)}$ - substituent cannot be explained by a steric effect. It is suggested that Grant and Cheney's[24] formula for γ shifts, which assumes a dominant hydrogen-hydrogen interaction mechanism, should be expanded to general electron-electron repulsion mechanism, as other polar groups cause similar, usually larger, shift changes in the <u>endo</u> case.

The γ- shifts at $C_{(6)}$ induced by <u>exo</u> - 2 - substitution were found to correlate with substituent electronegativity. Any tendency of the <u>endo</u> substituents to produce a similar change is occluded by the steric effects. $C_{(7)}$ and $C_{(4)}$ γ shifts exhibit no correlation with substituent electronegativity. The authors suggest that the special behaviour of <u>exo</u> - 2 - substituents is due to an effect similar to the W arrangement of atoms which gives rise to long range spin-spin coupling interactions, such that

overlap between the back lobes of $C_{(2)}$ and $C_{(6)}$ controls the value of the $C_{(6)}$ shift. As evidence they cite the similar upfield shifts found for ^{19}F chemical shifts in 4 substituted 1 - fluoro - bicyclo [2.2.2.] octanes[85] and shielding effects found for carbon nuclei in delocalised carbonium ions.[86]

A systematic study of the γ effect[87] has shown that for substituents which contain other elements in addition to carbon and hydrogen, greater upfield shifts are found for anti carbon atoms than for those gauche to the substituent. Clearly steric effects alone cannot account for these facts, and other mechanisms must be considered.

Mechanisms involving through the bonds or through space inductive or field effects are not applicable as there is no correlation with electronegativity or other inductive parameters. A mechanism involving back lobe W type interactions does not account for the fact that first row hetero atoms cause larger upfield shifts than those from the second row.

In order to rationalise the observations above, Eliel's group propose that a special mechanism exists for nitrogen, oxygen and fluorine bearing substituents, involving a hyperconjugative interaction between free electron pairs on these atoms and the C_α - C_β bond accompanied by subsequent alternation of electron density at the γ anti-periplanar carbon. The shorter length of the C - X bond in these atoms and the similar radial dimension to that of carbon favours this mechanism for first row hetero atoms but not for those of the second row, fig.6.

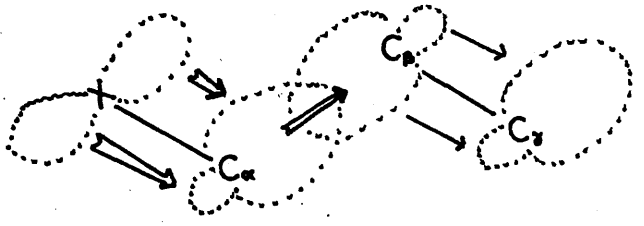


fig.6

It has been shown by low temperature ^{13}C n.m.r.[88] that, although axial substituents shield γ carbons in substituted cyclohexanes to a greater degree than equatorial substituents, the shielding does not increase with the effective size of the substituent as measured by the free energy difference between axial and equatorial substituted cyclohexanes, suggesting that sterically induced polarisation is not the dominant factor for the observed 1, 3 diaxial effects.

A study of the chemical shifts of bicyclo [2.2.1] heptanes[89] indicates that, in general, all the important effects are electronic in nature and the influence of the diamagnetic anisotropy of nearby chemical bonds and rings is shown by calculation to be negligible. It is found that the 1, 4 interaction between the ring and a substituent is not reciprocal. For 2-methyl norbornanes the δ effect is strongest on $C_{(6)}$, causing about twice the diamagnetic shift observed for $C_{(7)}$ and the methyl itself.

Methyl-substituted norbornanes[90] were used to study the effect of the dihedral angle of 1, 4 non-bonded interactions on the δ effect, since this angle is a relative measure of steric crowding. It was shown that a decrease in the dihedral angle between vicinal methyl groups causes an upfield shift. It is also illustrated that 1, 4 effects between two like groups, e.g. methyl groups, do cause reciprocal effects.

The α effect in 1-substituted adamantanes[91] is found to correlate well with that of the quaternary carbon in substituted t-butyl derivatives. The β effect is found to correlate with the methyl chemical shifts of t-butyl derivatives and the $C_{(2)}$, $C_{(6)}$ chemical shifts in 1-substituted cyclohexanes.[76]

In the discussion of β effects substituents are divided into two classes:-

Class I : those substituents containing only one atom heavier than hydrogen.

Class II : those substituents containing more than one atom heavier than hydrogen.

It is found that in all cases, Class I derivatives bring about more paramagnetic shifts at the β carbon than do Class II substituents. The most electronegative elements in Class I give rise to smaller paramagnetic effects, in agreement with the calculated alternating charges on carbon atoms in a ring system.

In Class II derivatives 1, 4 interactions between the β carbon and the second "heavy" atom of the substituent, e.g. oxygen in the nitro group, produce an upfield contribution to the total β effect; hence the β carbons resonate at high field when a Class II substituent is present.

The geometry of the adamantane system is such that there is a reduction in the non-bonded interactions between apical 1-substituents and the γ carbons and instead of the normally large diamagnetic γ shifts, paramagnetic shifts are observed.

A reasonable correlation exists between the inductive constant, σ^*, and the ^{13}C shifts of Class I compounds; the correlation improves if heavy halogen substituents are excluded.

High field δ shifts in adamantanes are found to correlate well with:-

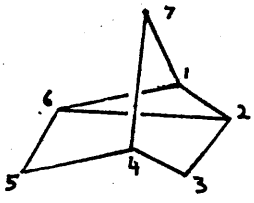
(i) the analogous δ shifts in cyclohexanes[76]
(ii) the inductive constant, σ^*

As for substituted cyclohexanes, Lippmaa's group attributed these trends to charge alternation, noting that the methyl group acts as an electron withdrawing group, in accordance with E.H.T. calculations.[78]

Maciel et al[92] redetermined the ^{13}C chemical shifts of 1-substituted adamantanes observing no major discrepancies with the earlier data. ^{13}C chemical shifts of 2-substituted adamantanes were also reported, the γ syn resonances in these compounds are assigned to higher field than γ anti on account of the greater 1, 4 interactions in the former case.

Maciel's group[93] also report the ^{13}C chemical shifts of five 1-substituted bicyclo - [2.2.2.] - octane derivatives. They note the correlation of $C_{(1)}$, $C_{(2)}$ shifts in these

compounds with the corresponding shifts in ethyl derivatives and point to the possible influence of a field effect on the shifts of $C_{(4)}$. However, owing to the small number and nature of the substituents chosen, it is not wise to read too much into these trends.



(10)

The high field shift observed for $C_{(4)}$ in nortricyclene[94] (10) relative to that found for $C_{(4)}$ in norbornane (9) is assigned to the effects non-bonded interactions between the cyclopropyl carbons and $C_{(4)}$ in (10). These interactions in (10) will be more pronounced than the corresponding interactions in (9) owing to the shorter non-bonded distances involved. By a similar argument, the downfield shift observed for the gem-dimethyl groups of tricyclene relative to those found in bornane are ascribed to the reduction, in the former case, of non-bonded interaction between ring methylene carbons and the syn methyl group.

Molecular orbital calculations have not proved very successful in the prediction of trends of substituent chemical shifts in aliphatic systems in terms of electron densities and little work has been published in this area.

By means of Extended Huckel Theory (E.H.T.) calculations[80] it has been shown that the carbon chemical shifts in mono-substituted methanes are approximately proportional to the gross atomic charges on the central carbon atoms with major deviations for substituents containing double bonds i.e. acetaldehyde and nitromethane, which they ascribe to multiple bond effects, in this case hyperconjugation; the double bonds are delocalised such that orbitals on the central carbon with the correct symmetry participate in them.

Linear correlations between the chemical shift of the central carbon in substituted methanes are also found using Del Re's parametric M.O.L.C.A.O. method[95] but a fairly wide spread of points are found using this method.

Miyajima and Nashimoto[96] report that the ^{13}C chemical

shifts of methyl, ethyl, n-propyl and butyl derivatives are qualitatively proportional to the σ electron density on each carbon as calculated by the σ - included ω - H.M.O. method.

In plots of the electron density of a given carbon and its chemical shift they find that the α effects of nitro, cyano, chloro, bromo and iodo groups give rise to significant deviations from linearity and no substituent effects are found for the δ carbon of n-butyl groups. They attribute deviations from linearity in the plots for carbons, observed for nitro and cyano, to anisotropy effects but the calculations do not account for the magnitude of this effect. Deviations from linearity, observed for the heavy halogen substituents, are said to be caused by the non-inclusion of d orbitals in the calculations.

II. Aromatic Systems.

A) Monosubstituted Benzenes.

^{13}C n.m.r. spectroscopy provides a useful probe for examination of the effects of a substituent on an aromatic system. Among the pioneers of this type of work were Spiescke and Schneider.[97] They found that the chemical shift of the substituent bearing ring carbon in mono-substituted benzenes correlated linearly with the Pauling electronegativity[36] of the substituent after correction for the substituent anisotropy.

The chemical shift of the ortho carbons cannot be fully accounted for since there are many factors, i.e. anisotropy, inductive and resonance effects which are operative at this position to a varying extent in different substituents.

No correlation is found with electronegativity or linear free energy parameter, σ_I, hence the inductive effect of the substituent is not important. There was no linear relationship between the chemical shifts of this carbon and Hammett constant, σ_M.

It is considered that at the para position the most important factor affecting the chemical shifts will be changes in π electron density brought about by the resonance effect of the substituent and reasonable correlation of para chemical shifts with the Hammett constant σ_p is found.

The uniformly small chemical shifts at the meta position have been taken as part of the evidence that the π inductive effect controls the ground state π electron density and hence the ^{13}C chemical shifts in monosubstituted benzenes.[98]

The only reported correlation[99] between meta chemical shifts and Hammett type parameters showed that meta chemical shifts were proportional to $\sigma_I - 0.7\sigma_\pi$ from which it was concluded that the resonance effect is positive at this position, i.e. opposite in direction to that at the para position; σ_π is a measure of the total π electronic effect.[100]

Maciel's group[101] has shown that the Taft resonance parameter σ_R^0 [47] correlates with the difference in the para and meta chemical shifts. This would be expected if the inductive effect and ring currents influence meta and para positions to the same degree.

There have been several attempts to relate the ^{13}C chemical shifts of monosubstituted benzenes to theoretically calculated electron densities. The earliest attempts at establishing relationships of this type used theories which only considered the π electrons. The chemical shifts of the para carbons were found to be linearly related to the calculated π electron densities.[102] However, no such correlation was found for the ortho or meta carbons.

It has been shown that the chemical shifts of benzene ring carbons are proportional to the total charge density, for each carbon atom, calculated using C.N.D.O. theory if all types of carbon atom are considered together.[103] If the chemical shifts of each carbon atom are plotted against their total electron density, only the para carbon chemical shifts show adequate correlation with the corresponding electron density.

Similar results have been found by other workers who used C.N.D.O./2 theory[104] and Del Re's parametric M.O.L.C.A.O. method.[105]

B) Disubstituted Benzenes.

After the publication of the chemical shifts of a wide range of aromatic carbonyl compounds in 1964[106], there have

been several systematic studies of substituent effects on particular types of carbonyl carbon.

For para substituted benzaldehydes[107] no correlations were found between the ^{13}C chemical shifts of the carbonyl carbon and the Hammett constants σ_P or σ_R^0 whereas the chemical shift of the formyl proton is found to be linearly related to σ_P.[108] It is suggested that the carbonyl carbon in para substituted benzaldehydes is not in the correct position in the molecule to be greatly affected by resonance effects hence there are no correlations found between the chemical shifts of the carbonyl carbons and σ_P or σ_R^0. No other single parameter has successfully correlated these shift trends.

For meta substituted benzaldehydes a linear relationship is found between the carbonyl chemical shifts and Hammett constant σ_M. This is taken to imply that the carbonyl chemical shifts of meta substituted benzaldehydes appear to be governed mainly by the effect the substituent has upon the conjugation between the aromatic ring and the carbonyl group.[107]

Linear relationships were found between the chemical shifts of the carboxyl carbon of meta and para substituted benzoic acids[109] and

(i) the pK_a values of the acids[110]

(ii) the π electron densities calculated by the I.N.D.O.[58] and C.N.D.O./2[57] methods

(iii) Hammett parameters[111]

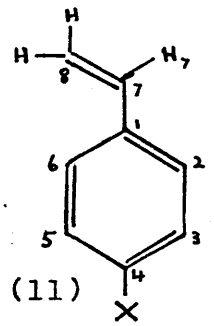
The only major deviations from these correlations were for strongly π donating para substituents, for which upfield shifts were found. In these compounds it is expected that the carboxyl group will conjugate fairly strongly with the benzene ring and carbonyl carbon chemical shifts are known to exhibit upfield shifts in a conjugative system.[1]

The cyano group is similar to the carbonyl group in that it has a strongly electron withdrawing effect on an aryl ring and contains a multiple bond in formal conjugation with the ring.

There are two reports of ^{13}C chemical shifts in meta and para substituted benzonitriles[112,113]; in the first[112] high concentrations of nitrile in several non-inert solvents

showed no discernible substituent trends. Bromilow and Brownlee,[113] using Taft's inductive and resonance parameters in a D.S.P. analysis[47] of the Substituent Chemical Shifts (S.C.S.), have shown that field effects have larger weighting than resonance effects at the cyano carbon in both meta and para series whereas for the ring carbons to which the cyano group is joined field effects are more important for the meta series but resonance effects, as for mono substituted benzenes, are more important than field effects in the para case.

Reynolds et al have measured ^{13}C, ^{1}H chemical shifts and performed electric field and M.O. calculations on substituted styrenes(11),[114,115] phenylacetylenes(12),[116] and phenylalkanes(13),[117] in terms of a D.S.P. treatment using F and R.[48]



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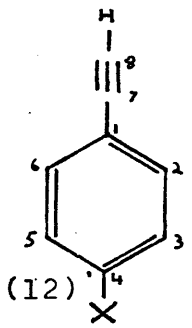

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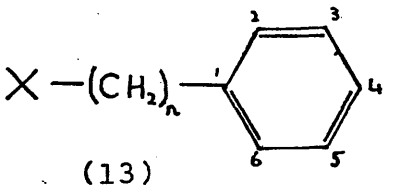


(13)

It was demonstrated[114] that S.C.S. values can be accounted for by a model in which the substituent effects are transmitted either through field effects, conjugative interactions or by polarisation of the styrene π electron system by the polar C - X bond (the π polarisation effect).

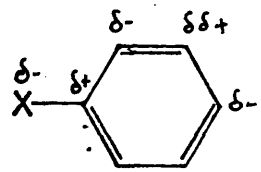
For α methyl or α t-butyl styrenes[115] where conjugation is inhibited by steric interactions, the vinyl and phenyl systems are independently polarised by through space interactions leading to equal changes in electron density at $C_{(7)}$ and $C_{(8)}$. For styrene itself which is planar the complete π system is polarised leading to transfer of electron density from $C_{(8)}$ to the ring with the electron density of $C_{(7)}$ remaining unchanged.

The results for substituted phenylacetylenes[116] indicate that an increased field dependence of the electron density and chemical shift of $C_{(8)}$ carbons in phenylacetylenes relative to styrenes[114] are attributable to increased π polarisation of the ethynyl group over that experienced in the vinyl group

of the styrenes. This is expected as a $-C\equiv C-$ bond is known to be more polarisable than a $-C=\!= C-$ bond. From the coefficient, r, of R for C_1 and $C_{(8)}$ in styrenes and phenylacetylenes it is concluded that the decreased r values found for $C_{(8)}$, and the increased r value of C_1 of phenylacetylenes relative to styrenes imply, that more of the resonance effect remains localised in the benzene ring in the phenylacetylenes than in the styrenes.

For substituted phenylalkanes[117] of the type (13) Reynolds' group proposes, that for a given pattern of chemical shifts on the ring carbons, it is possible to deduce the mode of electron transfer through the system.

In a dominant orbital repulsion mechanism (14)



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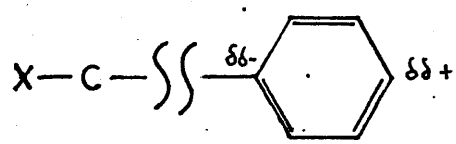


(15)

$C_{(2)}$ and $C_{(6)}$ should have similar shifts to $C_{(4)}$ with $C_{(3)}$ and $C_{(5)}$ of opposite sign.

They suggest that π polarisation effects show the pattern (15) and the chemical shifts and π electron densities in phenyl alkanes are consistent with this pattern. It is also concluded that an inducto-electromeric mechanism, where changes in the σ electron densities of the ring carbons bring about changes in the π electron density is not present as the π electron densities of the ring carbons are consistently greater than their σ counterparts.

In para substituted fluoro benzenes[118] the electron densities of particular ring carbons, as calculated by the σ included ω - H.M.O. method, correlates with ring carbon chemical shifts as follows:- the ring carbon α to the substituent with σ electron density; the ortho carbon with the π electron density and the meta and para carbon with the total electron density. However, on inspection there are some quite serious deviations from linear correlations especially for α and ortho substituents.

Lastly the chemical shifts of constituent carbons of

alkyl groups in simple and branched alkyl benzenes[119] have been shown to be predictable by the Grant and Paul approach.[61]

The methylene carbon chemical shifts of α-tolyl derivatives, $PhCH_2X$,[120] correlate with the electronegativity parameter, Ex.[121]

For the chemical shifts of the methoxyl carbons of substituted anisoles no marked substituent dependence was found.[122]

c) The chemical shifts of non carbon nuclei in aromatic side chains i.e. ^{19}F, ^{15}N, ^{14}N.

The ^{15}N chemical shifts of the amino nitrogen atom in meta and para substituted anilines[123] correlate with the π electron density of the nitrogen atom as calculated by Huckel theory, and with the chemical shifts of the amino protons. The ^{19}F chemical shifts of para substituted fluorobenzenes are also found to be approximately related to the π electron density on the fluorine atom.[118,124] The amino group and the fluoro group are both significant π electron donors to the para position, hence the correlations above are not unexpected.

The ^{19}F chemical shifts of meta substituted fluoro benzenes have a linear relationship with linear free energy parameter, σ_I,[124] but not with the σ electron density on fluorine. In the meta position fluorine will not be directly conjugated with the substituent, so a correlation involving a dominant inductive mechanism is not surprising. However, the fact that a linear relationship exists between the S.C.S. of meta substituted anilines and the π electron density is somewhat unexpected, as resonance interactions between the amino group and the substituent are improbable even though the amino group is strongly π donating.[123]

The results of ^{15}N chemical shifts of the nitro group in para substituted nitrobenzenes[125,126] indicate that the inductive effect of the substituent exerts the major influence on the magnitude of these shifts.[126] The evidence for this, albeit of a negative nature, is the lack of correlation of the shifts with the π electron density on the nitro nitrogen atom

and the superior correlation of these shifts with Hammett parameter σ_M over that with σ_P.

These findings agree well with ^{14}N chemical shift results which indicate that the effects of meta and para substituents on the nitrogen chemical shifts of nitrobenzenes are very similar.[127]

I.N.D.O. calculations on methyl-substituted anilines[128] show that, except for para methyl aniline, the ^{15}N chemical shifts correlate well with total electron density on nitrogen. Methyl substitution decreases the nitrogen π density and upfield shifts arise from larger increases in the σ electron density.

It is suggested that these shifts show a small upfield trend on account of an increase in the diamagnetic contribution and the ^{15}N chemical shifts of the polymethyl substituted anilines show different linear relationships with Hammett σ parameters from those bearing more electronegative substituents.

Comparison of the amino[123] and nitro[125] ^{15}N shifts indicates a partial correlation.[129] The increase in the amino shift of para nitroaniline over that predicted is consistent with that expected from enhanced delocalisation.

A plot of the ^{15}N shifts of anilines against those of nitrobenzenes for other substituents does not follow an order expected from a dominant inductive effect which were thought to control the ^{15}N chemical shifts of the nitro group in nitrobenzenes.[126] Good correlation is found in a D.S.P. treatment of the ^{15}N shifts of nitrobenzenes with both F and R[48] which indicates a previously unrecognised resonance component to nitrobenzene ^{15}N S.C.S.[129]

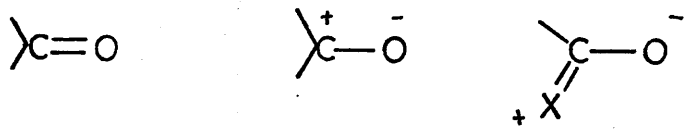
The ^{15}N chemical shifts[130] of the amino nitrogen in meta and para substituted benzamides and the nitrile nitrogen of para substituted benzonitriles both showed a linear relationship with the Hammett constant σ but poorer correlation was obtained when σ_p and σ_M were used in the apposite cases.

III Multiple bonded systems.

A) The Carbonyl Group.

Much of the interest in multiple bonded compounds has

centred on the carbonyl group. Generally the carbonyl carbon absorbs at lower field in the ^{13}C spectrum than other common functional groups primarily due to contributions from (17) caused by polarisation of the π bond in (16) towards oxygen.



(16) (17) (18)

Replacement of a hydrogen α to the carbonyl carbon by a methyl group causes a further downfield shift whereas a more electronegative group can conjugate with the carbonyl group causing a higher electron density on the carbonyl carbon owing to contributions from (18), bringing about an upfield shift. Thus amides and esters resonate at higher field than ketones and aldehydes.

Savitsky et al[131] have shown that, although the above argument is qualitatively correct, the S.C.S. on the ^{13}C chemical shifts of the carbonyl carbon do not follow a recognisable inductive order, in compounds of the type, $CH_3 - CO - X$.

Any correlation of chemical shifts and parameters representing electron density assumes that the average excitation energy, ΔE, which appears in Pople's expression for the paramagnetic shielding constant,[15] does not vary with change of substituent. Savitsky's group show that the energies of the $n \longrightarrow \pi^*$ transitions in the compounds $CH_3 - C(O) - X$ above are linearly related to the carbonyl carbon chemical shift as X changes, and high excitation energies cause high field shifts. If $n \longrightarrow \pi^*$ transitions in this series are representative of the mean excitation energy, ΔE, then this term and not the effect of electron density on $\left\langle \frac{1}{r^3} \right\rangle_{2p}$ is the dominant factor affecting carbonyl carbon chemical shifts.

It is also found that the $n \longrightarrow \pi^*$ transitions in unsubstituted bicyclic and cyclic aliphatic ketones[132] give a reasonable correlation with the carbonyl carbon chemical shifts which may explain some of the anomolies in

the rationalisation of the chemical shifts of these compounds by invoking "strain" effects.

The ^{17}O shifts of the carbonyl oxygen have also been shown to correlate with the $n \rightarrow \pi^*$ transitions in the same sense as for the carbonyl carbon.[133] This trend is general for most types of ketone and aldehyde, however in some ketones the ^{17}O chemical shifts[134] of the carbonyl oxygen are moved to low field by high excitation energies and a rationalisation is attempted in terms of increasing polarisation of the carbonyl grouping.

There is no linear relationship between the $n \rightarrow \pi^*$ transitions in substituted acetophenones[135] and the ^{17}O chemical shifts possibly due to the fact that $n \rightarrow \pi^*$ transition is not a good approximation to ΔE in aromatic systems as $\pi \rightarrow \pi^*$ transitions occur at similar energies. In this case, it is suggested that the $\langle r^{-3} \rangle_{2p}$ term dominates and the ^{17}O chemical shift is a function of the electron density on oxygen.

B) Other multiple bonded systems.

There have been several studies of the ^{13}C chemical shifts of systems containing two multiple bonds in series. For example:- allenes[136] of type $\begin{matrix} R \\ R \end{matrix}\!\!>C = C = C\!\!<\!\!\begin{matrix} R \\ R \end{matrix}$, ketenes,[137] $\begin{matrix} R \\ R \end{matrix}\!\!>C = C = O$, diazoalkanes[138] $\begin{matrix} R \\ R \end{matrix}\!\!>C = N = N$, ketenimines,[139] $\begin{matrix} R \\ R \end{matrix}\!\!>C = C = N - R$, where R is Me or H, and carbon suboxide,[140] $O = C = C = C = O$.

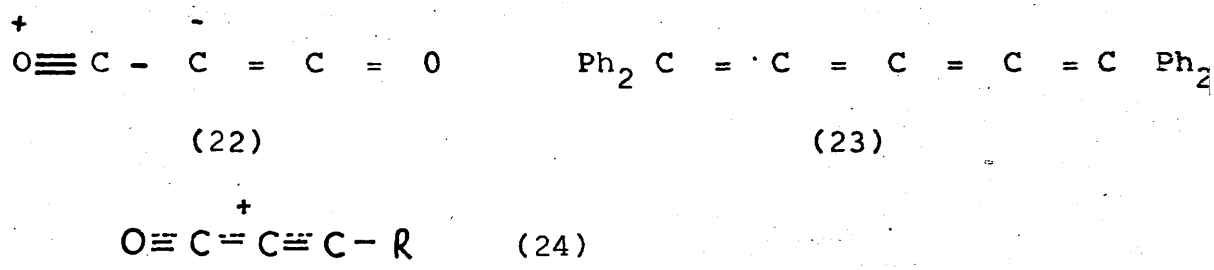
The trends in the C.N.D.O./2 electron densities for the central carbon of the allenes[136] are in good agreement with the trends in the chemical shifts. The central carbon in ketene[137] resonates at lower field than carbon monoxide and is found in the region expected for metal carbonyls, implying that the carbon oxygen bond in ground state ketene has some triple bond character and involves a predominant weighting of (19) and the analogous form (20)

$\rangle \overset{-}{C} - C \equiv \overset{+}{O}$ (19) $\rangle \overset{-}{C} - \overset{+}{N} \equiv N$ (20) $\rangle \overset{-}{C} - X \equiv \overset{+}{Y}$ (21)

is the best description of ground state diazoalkanes.[138]

The central carbon, $C_{(1)}$ in carbon suboxide (22)[140] is one of the most shielded carbons reported to date (-14.6 p.p.m.). The high field shift on this carbon is rationalised by comparison of its chemical shift and total charge density with those of the analogous carbon in a series of cumulenes (23)[141] and the high field shift is thought to be due to high charge density on $C_{(1)}$ of carbon suboxide.

The carbonyl carbon chemical shift of carbon suboxide is at higher field than that of ketene. The situation in this case(22) is compared to that in alkynol cations[142](24) where formation of cations shielded the carbonyl and its α carbon. The facts are



(22) (23)

consistent with major contributions arising from resonance forms such as (22).

The chemical shifts of the S_p2 terminal carbons in allenes give poorer correlation with calculated charge densities than was found for the central carbon, however better agreement is found when a correction is made for the diamagnetic term.[17] The higher electron density found on the S_p2 terminal carbon of ketene with respect to those in allene is in accord with the high field shifts found in the ketene case.

The terminal carbons in ketenimines and diazoalkanes resonate in the same region of ^{13}C spectrum as those of ketene. If the excitation energy in allenes, ketenes, diazoalkanes and ketenimines is assumed constant the differences in terminal carbon chemical shift is attributed to a higher π electron density on the terminal carbon in the other three compounds with respect to allene. The σ density in all four types of compound is not thought to vary much as the value of J_{C-H} for the terminal carbon in each series is about the same ca. 170 Hz.

The importance of this high π electron density in the latter three compounds above is manifested in the predominant weighting of resonance forms of the type (21) in these three compounds.

EXPERIMENTAL.

Melting points (m.p.) were recorded on a Kofler microscope hot stage, are uncorrected and quoted in ^{o}C.

Routine infra-red (i.r.) spectra (Nujol mulls, liquid films) were recorded on Pye Unicam S.P. 1000 or Perkin Elmer 257 spectrophotometers; carbon tetrachloride solution ($C Cl_4$) and potassium bromide disc (KBr) i.r. spectra were recorded on a Perkin Elmer 225 spectrophotometer.

Ultra-violet (u.v.) spectra were measured on a Pye Unicam S.P.800 spectrophotometer as solutions in 95% ethanol. Extinction coefficients, ε, are placed in brackets.

^{1}H nuclear magnetic resonance (n.m.r.) spectra were recorded on Varian T-60 and HA-100 instruments with $CDCl_3$ as solvent and T.M.S. as internal standard. ^{13}C spectra were recorded on Varian XL-100 and CFT 20 or Brucker HFX 13 spectrometers using approximately 0.5M solutions of $CDCl_3$. The latter instrument was used for ^{15}N spectral determinations.

Mass spectra (m.s.) were recorded on a G.E.C. - A.E.I. M.S.12 spectrometer. The molecular ion (M^+) is quoted first in all cases.

Microanalyses were carried out by Miss F.Cowan and Mrs.W.Harkness at the University of Glasgow.

Thin layer chromatography (t.l.c.) was carried out using Kieselgel G (Merck) for analytical purposes and Kieselgel HF_{254} for preparative work, eluting solvents are in brackets.

Solvents were routinely dried using anhydrous sodium sulphate and were removed on a rotary evaporator at reduced pressure.

Abbreviations	b	broad
	d	doublet
	m	multiplet (in n.m.r.)
		medium intensity absorption (in i.r.)
	q	quartet
	s	singlet (in n.m.r.)
		strong intensity absorption (in i.r.)
	t	triplet
	w	weak intensity absorption.

I. Preparation of 1- substituted camphenes

Camphor oxime.

Camphor (100g, 0.66 mol.) in ethanol (300 ml), hydroxylamine hydrochloride (100g, 1.42 mol.) in water (200 ml), and sodium acetate trihydrate (123g, 0.9 mol.) were refluxed together for five hours. The cooled solution was poured into water (1.5 ℓ) and the product filtered and washed with water until neutral giving crude camphor oxime, which was recrystallised from ethanol giving pure camphor oxime (135g, 80%), m.p. 118-9°. (lit.,[143] 118°)

2-Bromo - 2-Nitrobornane

This material was prepared by the method of Lipp.[144] Recrystallisation from ethanol gave white crystals which melted over a wide range, 202-215°, as they are a mixture of epimers.

1-Nitrocamphene (44)

The procedure used was that of Larsen,[145] recry stallisation three times from ethanol gave white crystals which melted at 54-55° (lit.,[145] 56°)

1-Aminocamphene[146] (37)

To a stirred solution of 1-nitrocamphene (1.5g, 8 mmol) in 50 ml of anhydrous ether contained in a 100 ml flask and cooled in an ice bath, was added in small portions excess lithium aluminium hydride (ca. 1g). Gentle reflux occurred after each addition; the solution was left stirring overnight. After the solution had been carefully poured into ether (150 ml), a saturated aqueous solution of sodium sulphate was gradually added to the ether until no further effervescence occurred. The solution was filtered and dried. Removal of solvent gave 0.8g of an oily product, which was purified by t.l.c. (ethyl acetate) ; bands between R.F. 0.1 and 0.4 were extracted giving 1-aminocamphene (0.42g, 33.5%), $\upsilon_{max.}$ (liquid film) 3450-3250, 890 cm^{-1}.

1-Hydroxycamphene[146] (38)

To a cooled stirred solution of 1-aminocamphene (1g, 6mmol.) in excess glacial acetic acid (15 ml), sodium nitrite (1.0g, 14 mmol.) was added in small portions. The solution was left stirring for 2h and was then poured into

water (200 ml) and brought to pH 9 by successive use of sodium hydroxide and sodium bicarbonate, extracted with ether (2 x 80 ml), and dried. Removal of solvent gave 1-acetoxycamphene 780 mg, $\nu_{max.}$ (liquid film) 1765, 890 cm^{-1}, which was used directly in the next stage.

1-acetoxycamphene was routinely reduced using lithium aluminium hydride using the same procedure as for (37). Removal of solvent gave crude 1-hydroxycamphene, which was purified by t.l.c. (5% ethyl acetate - 95% petrol). Extraction of the bands between R.F. 0.5 and 0.6 gave pure 1-hydroxycamphene (250 mg, 21%), $\nu_{max.}$ (CCl_4 : 0.05M) 3605 cm^{-1}.

Camphene - 1 - carboxylic acid (41) and camphene - 1 - carboxamide (42)

The method of Bergmann[147] et al was used to prepare these compounds.

1-Hydroxymethylcamphene (40)

Camphene - 1 - carboxylic acid (1.5g, 8 mmoles) was routinely reduced using lithium aluminium hydride in the method employed in the preparation of (37). Removal of solvent gave 1-hydroxymethylcamphene (750 mg, 52%) which, after recrystallisation from n-hexane had m.p. 35-36° (lit.,[148] 35-7), $\nu_{max.}$ (CCl_4 : 0.05M) 3639 (free OH) and 3600 cm^{-1} (intramolecular hydrogen bonded OH).

Methyl camphene - 1 - carboxylate[21] (43)

Nitrosan (10g) is covered with digol (20 ml), ether (150 ml) was added followed by a 30% aqueous solution of potassium hydroxide (30 ml). The temperature of the reaction quickly rises and ether and diazomethane distil into a cooled receiving flask containing ether (100 ml). The distillation is assisted by heating the reaction vessel with warm water until the yellow colour disappears. The ethereal solution of diazomethane is added to a solution of camphene - 1 - carboxylic acid (1g) in ether (20 ml) containing methanol (2 drops) until a permanent yellow colouring is obtained. Removal of solvent gave methyl camphene - 1 - carboxylate as a sweet smelling oil $\nu_{max.}$ (liquid film) 1750, 890 cm^{-1}.

1-Methylcamphene (36)

Magnesium turnings (9.5g, 0.4 atom) were washed in ether,

dried in a hot oven for thirty minutes, and then flamed in a flask under nitrogen for one minute. After cooling to room temperature, ether 50 (ml) was added, followed by methyl iodide (60 ml, 0.42 mol) which was added slowly with stirring until the reaction commences. The flask is then cooled while the remainder of the methyl iodide was added.

Camphor (15g, 0.1 mol.) dissolved in excess ether was added slowly, with stirring, to the mixture : care was taken to exclude all moisture. The reaction mixture, which was cooled in ice to prevent refluxing, was left for twenty four hours under a nitrogen atmosphere. Excess Grignard reagent was destroyed using a saturated aqueous sodium sulphate solution. The mixture was extracted into ether, dried and the removal of solvent gave 1-methylcamphene (6g, 40%) which, after recrystallisation from n-hexane, had m.p. 41-42° (lit.,[148] 43°).

1-Chlorocamphene (39)

This was prepared by the method of Joshi and Warnhoff.[149]

Preparation of 4-substituted-Isoborneols
4-Chloroisoborneol, 4-nitroisoborneol, isoborneol - 4 - carboxylic acid.

The method of Bergmann[21] et al was employed to prepare these compounds. The reaction of the 1-substituted camphenes with trichloroacetic acid was carried out at 60-70°C for 5h in the case of 1-chlorocamphene and camphene - 1 - carboxylic acid and at 100° for 15h in the case of 1-nitrocamphene. The trichloroacetates were obtained as oils and were used in the next stage without further purification. 4-nitroisoborneol trichloracetate showed $\upsilon_{max.}$ (film) 1760, 1535, 1380 and 1245 cm^{-1}.

Saponification of the trichloracetate was carried out as in the method of Bergmann.[147] Removal of the solvent gave the 4-substituted isoborneol in greater than 70% yield, recrystallisation from ethanol gave 4-chloroisoborneol m.p. 233-4 (lit.,[150] 235-6°) isoborneol - 4 - carboxylic acid m.p. 229-30° (lit.,[147] 230-231°) and 4-nitroisoborneol m.p. 266-7° (sealed capillary), $\upsilon_{max.}$ (nujol) 3430 br, 1540 and 1395-1370 cm^{-1}, δ ($CDCl_3$; Varian T60) 3.67-3.99

(endo - 3 - H) (Found : C, 60.1 ; H, 8.4 ; N, 6.4. $C_{10}H_{17}NO_3$ requires C, 60.3 ; H, 8.6 ; N, 7.05%).

4-Bromoisoborneol.

This compound was prepared by the method of Wassmundt.[151]

Preparation of 4-substituted camphors

4-Chlorocamphor (51) 4-bromocamphor (52) 4-nitrocamphor (53), camphor - 4 - carboxylic acid (49)

These compounds were prepared from the relevant 4-substituted isoborneol by the method of Bergmann.[147] Removal of solvent and recrystallisation from ethanol gave the pure 4-substituted camphor in greater than 80% yield; camphor - 4 - carboxylic acid, m.p. 238- 9° (lit., [147] 239-40°), 4-chlorocamphor, m.p. 197-8 (lit., [150] 198-9°), 4-bromocamphor, m.p. 194-5° (sealed capillary), $\upsilon_{max.}$ (CCl_4) 1754 cm^{-1} (Found : C, 52.03 ; H, 6.53. $C_{10}H_{15}BrO$ requires C, 51.97 ; H, 6.54%) and 4-nitrocamphor m.p. 220-221°, δ ($CDCl_3$) 0.95 (3H,s), 1.00 (3H,s), 1.12 (3H,s), 3.26 (exo - 3 - H) and 2.55 (endo - 3 - H) (A B, J_{AB} 18.0 Hz) (low-field component, exo - 3 - H, further split by coupling with exo - 5 - H, J 3.85 Hz) (Found : C, 60.8 ; H, 7.65 ; N, 7.2. $C_{10}H_{15}NO_3$ requires C, 60.9 ; H, 7.65 ; N, 7.1%).

Camphor - 4 - urethane

The method of Weinstock[152] was used to prepare this compound.

4 - Aminocamphor (47)

4-Aminocamphor was obtained from camphor - 4 - urethane using the method of Houben.[150]

4 - Hydroxycamphor (48)

Sodium nitrite (2.6g, 4 mmol) in water (10 ml) was added to a solution of 4 - aminocamphor (2.5g, 16.5 mmol) in water (22 ml.) and glacial acetic acid (5 drops). The mixture which became cloudy after 1h was allowed to stand at 25° for 4h. The acidic solution was extracted with pentane (3 x 50 ml.) and the combined organic layers were dried. Removal of solvent

gave 4-hydroxycamphor (1.1g) which on recrystallisation from benzene had m.p. 248-9° (lit.,[150] 250°)

Camphor - 4 - carboxamide (50)

To a stirred solution of camphor - 4 - carboxylic acid (4.7g, 25 mmol) in benzene (25 ml) at room temperature, with protection from moisture, was added oxalyl chloride (7.5g, 59 mmol). Stirring was continued for 4h at room temperature. Benzene was then removed by distillation and the solution kept 40 min (0.1 mm) leaving camphor - 4 - carbonyl chloride as a colourless oil, $\upsilon_{max.}$ (film) 1780, 1750 cm^{-1}. The crude acid chloride was dissolved in ether (50 ml) in a three necked flask and excess gaseous ammonia was passed through the solution. Solvent was removed leaving camphor - 4 - carboxamide (3.9g, 70%) a white solid which after recrystallisation from ethanol melted at 205-6° (lit.,[150] 207-208°).

4-Acetylcamphor (55)

To a solution of isoborneol - 4 - carboxylic acid (1.98g, 10.0 mmol) in anhydrous tetrahydrofuran (50 ml) contained in a 100 ml 3-necked round bottomed flask maintained under an atmosphere of dry nitrogen was added by injection through a serum cap a solution of methyl lithium in hexane (Lithium Corporation of America) (14.5 ml of a 2.1 M solution in hexane, 30.5 mmol). The resultant solution was stirred overnight. After cautious addition of water (20 ml) and extraction with ether, the organic layer was dried, and the solvent removed. The 4-acetyl isoborneol so obtained (1.70g) was directly oxidised with Jones reagent using the method of Bergmann.[147] This procedure yields 4-acetylcamphor (1.52g, 78% from 4-isoborneol carboxylic acid). On recrystallisation from Analar petroleum ether (60-80°) this material had m.p. 48°, $\upsilon_{max.}$ (CCl_4) 1750, 1719, 1698 cm^{-1}.

Methyl camphor -4 - carboxylate (54)

This compound was prepared from camphor - 4 - carboxylic acid by treatment with diazomethane as for (43) to give a sweet smelling oil which solidifies on standing for several weeks and had m.p. 39° (Found : C, ; H, . $C_{12}H_{18}O_3$ requires C, 68.55 ; H, 8.36%), $\upsilon_{max.}$ 1752 cm^{-1}.

Preparation of 4-substituted Camphor p-tolylsulphonylhydrazones
Camphor p-tolylsulphonylhydrazone, 4-chlorocamphor p-tolylsulphonylhydrazone, 4-nitrocamphor p-tolylsulphonylhydrazone.

Camphor derivatives (ca. 10g) and an equimolar amount of p-tolylsulphonylhydrazine were dissolved in the minimum amount of warm ethanol and concentrated hydrochloric acid (4 drops) was added. The solution was refluxed for 30 min; on cooling, crystals separated. These were filtered and recrystallised from ethanol to give the p-tolysulphonylhydrazone in 85% yield: camphor p-tolylsulphonylhydrazone, m.p.163-4° (lit.,[162] 163-4°) : 4-chlorocamphor p-tolylsulphonylhydrazone, m.p. 197-8° (Found : C, 57.8; H, 6.7; N, 7.95. $C_{17}H_{23}ClN_2O_2S$ requires C, 57.55; H, 6.55; N, 7.9%), 4-nitrocamphor p-tolylsulphonylhydrazone, m.p. 210° (Found : C, 56.0; H, 6.35; N. 11.5. $C_{17}H_{23}N_3O_4S$ requires C, 55.9; H, 6.35; N, 11.5%).

Preparation of 4-substituted Tricyclenes
Tricyclene (25), 4-chlorotricyclene (32)
4-nitrotricyclene (33).

Into a three necked 250 ml round bottomed flask were placed the camphor p-tolylsulphonylhydrazone (14.8 mmol) and dry tetrahydroforan (80 ml). The stirred slurry was maintained under dry nitrogen and a solution of methyl-lithium in hexane (Lithium Corporation of America; 7 ml of a 2.1 M solution, 14.2 mmol) was injected through a serum cap. The temperature was kept at 0-5° during addition and for 30 min. thereafter. After 30 min. at room temperature the solvent was removed at 40°. The resulting salt was pyrolysed at 200° and the tricyclene was swept into a dry-ice trap by the nitrogen stream with warming of the tube from the reaction flask to the dry ice trap. Tricyclenes were removed from the trap with pentane which was removed at 10°. Small amounts of olefinic material in tricyclene and 4-chlorotricyclene (n.m.r.) were removed by chromatography on a silver nitrate-alumina (Woelm neutral, grade 3) column.[163] Tricyclenes were preferentially eluted with pentane. 4-nitrotricyclene was

purified by recry stallisation from ethanol. Tricyclene had δ ($CDCl_3$) 0.82 (8H, s, 2 x CH_3 and cyclopropyl protons), 1.01 (3H, s), 1.66 (2H) and 1.03 (2H) (AB, J_{AB} 10.4 Hz), and 1.40 (1H, s). The absorptions for the AB pattern and the bridgehead C(4) proton were broad. 4-chlorotricyclene had δ ($CDCl_3$) 0.86 (6H,s), 0.98 (2H,s), 1.08 (3H,s), 1.95 (2H) and 1.56 (2H) (AB, J_{AB} 10.1 Hz). It was not possible to obtain a satisfactory microanalysis for this material because of its volatility (Found : C, 69.1; H, 9.0%; M^+ 170, 172. $C_{10}H_{15}Cl$ requires C, 70.35; H, 8.85%; M, 170, 172). 4-nitrotricyclene had m.p. 135-6°, δ ($CDCl_3$) 0.99 (6H,s), 1.09 (3H,s), 1.12 (2H,s) and 2.40 (2H) and 1.85 (2H) (AB J_{AB} 10.6 Hz) (Found : C, 66.15; H, 8.45; N, 7.8. $C_{10}H_{15}NO_2$ requires C, 66.25; H, 8.35; N, 7.75%).

4-Aminotricyclene (34)

This compound was prepared by treatment of an ethereal solution of 4-nitrotricyclene (2.3g) with lithium aluminium hydride as for (37) to give 4 aminotricyclene (1.25g, 65%) as an unpleasent smelling waxy solid, (CCl_4) 0.73 (6H,s), 0.85 (2H,s), 1.03 (3H,s) and 1.58 (2H) and 1.23 (2H) (AB, J_{AB} 10.1 Hz).

4-Hydroxytricyclene (28), 4-acetyltricyclene (31), tricyclene 4-carboxylic acid (29).

The method of Bergmann[147] was employed in the preparation of these compounds.

4-Hydroxymethyltricyclene (27)

Tricyclene - 4 - carboxylic acid (300 mg, 1.67 mmol) was routinely reduced with lithium aluminium hydride as for (37). Removal of ether gave 4-hydroxymethyltricyclene (251 mg, 91%) as a solid. Recrystallisation from the minimum volume of light petroleum (b.p. 60-80°) gave an analytical sample, m.p. 141-142°, ($CDCl_3$) 0.80 (6H,s), 0.91 (2H,s), 1.03 (3H), 1.59 (2H) and 1.20 (2H) (AB, J_{AB} 10.0 Hz), 1.32 br (1H,s, exchangeable with D_2O), and 3.72 (2H,s) (Found : C, 79.3; H, 10.75. $C_{11}H_{18}O$ requires C, 79.45; H, 10.9%).

4-Methyltricyclene (26)

To a solution of 4-hydroxymethyltricyclene (400 mg,2.41 mmol)

in anhydrous pyridine (8 ml) at 0° was added p-tolylsulphonychloride (476 mg, 2.5 mmol). The solution was stirred for 2 days and then poured into ice water; 2N hydrochloric acid was added with rapid stirring until the solution attained pH2. After extraction (3 x 100 ml) with pentane-ether (30 : 70), the combined extracts were washed with sodium hydrogen carbonate solution; solvent was removed to give 4 - p - tolylsulphonyloxymethyltricyclene (755 mg).

An ethereal solution of the sulphonate and lithium aluminium hydride (ca. 200 mg) were reacted together in a manner analogous to that used for (37), except that ether was removed at 10°. The crude product (26) is obtained as a waxy off-white solid, was chromographed on alumina (Woelm neutral, grade 3); elution with n-pentane gave pure 4-methyltricyclene [240 mg, 66.3% from (27)] as a waxy solid, m.p. 110-1° (sealed capillary), δ ($CDCl_3$) 0.70 (6H,s), 0.82 (2H,s), 0.89 (3H,s) and 1.04 (3H,s) and 1.45 and 1.55 A part of an AB pattern (the B part of this pattern was obscured by the methyl absorptions) J_{AB} 10.0 Hz. It was not possible to obtain a satisfactory microanalysis for (26), presumably on account of its volatility (Found : C, 85.65; H, 11.8%; M^+, 150. $C_{11}H_{12}$ requires C, 88.0; H, 12.0%; M, 150).

Methyl tricyclene - 4 - carboxylate (30)

A solution of tricyclene - 4 - carboxylic acid was methylated with diazomethane as for (43). The ester was obtained as a sweet smelling oil which on prolonged standing crystallised to a low melting solid, δ ($CDCl_3$) 0.90 (6H,s), 0.95 (2H,s), 1.04 (3H,s), 2.01 (2H) and 1.43 (2H) (AB, J_{AB} 10.0 Hz and 3.66 (3H,s).

Preparation of 4-substituted camphoroximes

4-methylcamphoroxime, 4-chlorocamphoroxime. camphoroxime - 4 - carboxylic acid, 4 nitrocamphoroxime.

These compounds were prepared from the camphor derivative in a manner analogous to that used in the preparation of camphor oxime, and used in the next stage without further purification.

Preparation of 4-substituted-camphornitrimines

Camphornitrimine (67), 4-methylcamphornitrimine (68) 4 nitrocamphornitrimine (69), 4-chlorocamphornitrimine (70), camphornitrimine 4-carboxylic acid (71).

These compounds were prepared, by the method of Brooks[153], from the relevant camphoroxime, giving; camphornitrimine which had m.p. 41-42° (lit.,[153] 41-43°); 4-methylcamphornitrimin m.p. 61-2° (Found : C, 62.84; H, 8.53; N, 13.42. $C_{11}H_{18}N_2O_2$ requires C, 62.83; H, 8.63; N, 13.32%). $\upsilon_{max.}$ (K Br) 1645 (m), 1560 (s), 1310 (s) cm^{-1}. 4-chlorocamphornitrimine m.p. 84-5° (Found : C, 52.17; H, 6.72; N, 12.40. $C_{10}H_{15}ClN_2O_2$ requires C, 52.2; H, 6.52; N, 12.14%) $\upsilon_{max.}$ (K Br) 1649 (m), 1570 (s), 1313 (s) cm^{-1}. Camphornitrimine - 4 - carboxylic acid m.p. 184-5° (Found : C, 54.99; H, 6.71; N, 11.66. $C_{10}H_{15}N_3O_4$ requires C, 55.17; H, 6.54; N, 11.58%) $\upsilon_{max.}$ (K Br) 1647 (m), 1568 (s), 1308 (s) cm^{-1}. 4-nitrocamphornitrimine, m.p. 144-5° (Found : C, 50.05; H, 6.40; N, 17.25. $C_{10}H_{15}N_3O_4$ requires C, 49.79; H, 6.27; N, 17.42%) $\upsilon_{max.}$ (K Br) 1650 (m), 1578 (s), 1537 (s), 1310 (s) cm^{-1}.

Pinacolone oxime.

This compound was prepared as described in Organic Synthesis.[154]

Pinacolone nitrimine (72)

The method of Suggit[155] was used to prepare this compound from pinacolone oxime.

Fluorene hydrazone.

This compound was prepared from fluorenenone employing the method of Staudinger.[156]

Diazofluorene (76)

Fluorene hydrazone was converted to diazofluorene by the method of Staudinger.[156]

Fluorenone nitrimine (73)

This compound was prepared from diazofluorene by the method of Horner.[157]

Preparation of diazocamphors.

4-Methylcamphorquinone

This compound was prepared by the method of Simonsen.[158] Recrystallisation of the crude product from light petroleum (b.p. 40-60°) gave 4-methylcamphorquinone m.p. 125-7° (Found : C, 73.35; H, 9.00. $C_{11}H_{16}O_2$ requires C, 73.30; H, 8.95%).

4-Methylcamphorquinone mono p-tolylsulphonylhydrazone.

4-methylcamphorquinone (3.0g, 16.6 mmol) was refluxed with p-tolylsulphonylhydrazone (3.14g, 16.9 mmol) in ethanol for 30 min. On cooling the mono - p - tolylsulphonylhydrazone separated (5.5g, 95%). Recrystallisation from methanol gave white needles m.p. 188-90° (Found : C, ; H, ; N, . $C_{18}H_{24}N_2O_3$ requires C, 62.13; H, 6.95; N, 8.05%).

4-Methyl - 3 - diazocamphor (74)

This was prepared from 4-methylcamphorquinone mono p-tolylsulphonylhydrazone by the method of Wiberg et al[159] to yield yellow crystals m.p. 95° (Found : C, 69.00; H, 8.59; N, 14.73. $C_{11}H_{16}N_2O$ requires C, 68.72; H, 8.39; N, 14.57%) $\nu_{max.}$ (nujol) 2100 1705 cm^{-1}.

Iso-nitrosocamphor

This compound was prepared by the method of Forster.[160]

Di-(3-aminocamphor) oxalate

Isonitroso camphor was converted, by the method of Duden et al[161], to 3-aminocamphor, and this was converted to its oxalate salt, di-(3-aminocamphor) oxalate.

3-Diazocamphor - $^{15}N(2)$

To di-(3-aminocamphor oxalate (1g) dissolved in water (10 ml) was added pentane (40 ml) and then slowly with stirring a mixture of unlabelled sodium nitrite (400 mg) and ^{15}N labelled sodium nitrite (100 mg) (Prochem Ltd.). The solution was stirred for 15 min. during which time the pentane layer turned yellow. After removal of the aqueous layer, the organic layer was washed with sodium bicarbonate solution and dried. Removal of solvent gave 3-diazocamphor - $^{15}N(2)$ (900 mg) which had m.p. 72-73° (lit.,[165] 74°C) $\nu_{max.}$ (CCl_4) 2080, 1695 cm-1.

Preparation of 3-3 di-deuterio 4-substituted Camphors

3-3 di-deuterio 4-chlorocamphor (64), 3-3 di-deuterio 4-methylcamphor (63), 3-3 di-deuterio 4-nitrocamphor (65)

Sodium (0.13g.) was added cautiously to methanol - $^2H_4$ (99% Prochem Ltd.) (4 ml), with initial external cooling in ice. To the resulting solution was added the 4-substituted camphor (51) (46) (53) (5 mmol) and deuterium oxide (1 ml). This solution was set aside at room temperature for four weeks. After successive addition of pentane (20 ml) [for (65) a 1:1 pentane-ether mixture was employed] glacial acetic acid (350 ml) and water (3 ml) were added, and the pentane layer further extracted with water. The organic layer was then dried and the solvent removed leaving the di-deuterated camphor. Mass spectral analysis showed for (63); 0% d_0, 2% d_1, 98% d_2: for (64); 0% d_0, 2% d_1, 98% d_2: for (65); 0% d_0, 1.5% d_1, 98.5% d_2.

Norcamphor-3 exo d_1 (66)

This compound was prepared by the above method with an exchange time of 23 min. Mass spectral analysis showed: 5% d_0, 92% d_1, 3% d_2.

Preparation of 1′, 1′ dimethyl 2′-benzoylhydrazides (97) - (115), 1′, 1′ dimethyl 2′-cinnamoylhydrazides (166) - (173) 1′, 1′ dimethyl phenylacylhydrazides (174) (180).

A solution containing N-N dicyclohexylcarbodiimide (12.3g, 60 mmol) and 1, 1 dimethylhydrazine (3.6g, 60 mmol) in methylene chloride (240 ml) was treated with the carboxylic acid (60 mmol). The solution was stirred overnight at room temperature and the N-N dicyclohexylurea preciptate was removed by filtration. The solution remaining was reduced in volume to ca. 50 ml, acidified to pH 1 and the methylene chloride layer removed. The aqueous layer was filtered by gravity until a clear solution was obtained. This was brought to pH 11 by the addition of sodium hydroxide pellets and extracted with methylene chloride (2 x 150 ml), giving an oil which usually crystallised on standing.

Footnote: In the compounds (87)-(115) the numbers 1′, 2′ refer to the nitrogen atoms of the O = C - N - N moiety.

The hydrazides were purified by recrystallisation from ethyl acetate. Analysis data on the hydrazides is given in Tables (4), (6), (8), (10).

Preparation of 1′, 1′, 1′-trimethylammonio 2′-benzimides (78) - (96) 1′, 1′, 1′-trimethylammonio2′- cinnamimides (151) - (158) 1′, 1′, 1′ trimethylammonio 2′-phenylacetimides (159) - (165)

Equal weights of the hydrazide (97 - 115) (166 - 180) and methyliodide were stirred together at room temperature, after sufficient chloroform had been added to complete the solution. After several hours a hydraziniumiodide salt precipitated from the reaction and was removed by filtration. The hydraziniumiodide salt was dissolved in an equimolar quantity of N sodium hydroxide and extracted into chloroform (2 x 200 ml). The combined chloroform washings were filtered by gravity until the solution became clear. Removal of solvent gave the trimethylammonio ylide which was purified by recrystallisation from ethyl acetate. Analysis data is given in Tables (5), (7), (9) and (11).

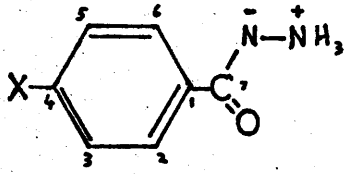
Preparation of meta and para-substituted Acetophenones (116) - (133)

These compounds were prepared from the substituted benzoic acid by the method employed for (55). The crude acetophenones were purified by recrystallisation from ethyl acetate if crystalline while oils and low melting solids were purified by t.l.c. in the appropriate mixture of ethyl acetate - petroleum ether (b.p. 40 - 60°) (see Table(12). This yielded three distinct bands, the middle one containing the pure acetophenone. The yield from the reaction was ca. 50% in each case. Analysis data for meta and para substituted acetophenones is contained in Table (12).

Calculation of the geometries of molecules for use in molecular orbital programs.

In general, standard (STD) bond lengths and angles were used in the calculation of molecular geometries except in the cases detailed below;

(i) Non-aromatic systems: The geometries of the camphor and tricycyl skeletons were obtained from x-ray studies of



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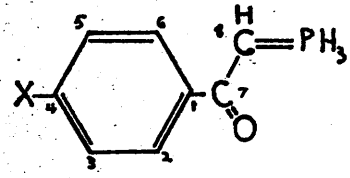

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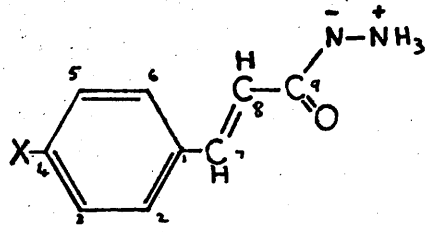

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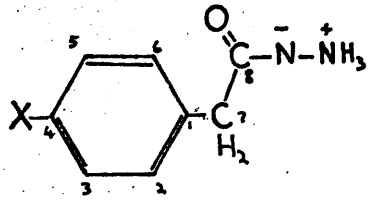


(184)

3-endo-bromocamphor[165] and 1-chloronortricyclene[166] respectively.

(ii) Aromatic systems: In compounds containing a benzene ring, it was assumed that the ring lies in the x, y plane of a cartesian co-ordinate system. Consequently, substituent effects occurring in the z planes are called π effects, while those occurring in the x, y plane are called σ effects.

Instead of using 1′, 1′, 1′-trimethylammonio 2′-benzimide (88), we employed structure (181) which contains an ammonio group rather than a trimethylammonio group in order to simplify the calculation of molecular geometry. The bond lengths of the O = C - N - $N(H_3)$ group were those determined in an x-ray study of (88).[167]

In our calculations on para-substituted styrene (11) derivatives, STD geometry was used except for the C(1) - C(7) - C(8) angle which was taken to be 128° as calculated by Pople.[168]

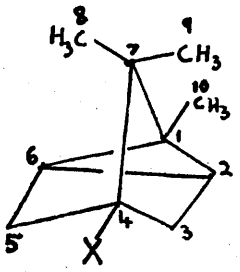
The geometry of the 1′, 1′, 1′-trimethylamine 2′-cinnamimide (151) was assumed to be composed of a combination of styrene and the O = C - N - $N(H_3)$ group from (181).[167]

Bond lengths and angles for the geometry of the acetyl group in acetophenone were taken from an x-ray study of para-nitroacetophenone.[169]

The geometry of the triphenylphosphonium ylide (134) is unknown. We considered the molecule to be planar owing to its similarity to acetophenone. STD bond angles were used and the bond lengths of C(1) - C(7), C(7) - C(8) and C(8) - P were taken from ref.170. A phosphonium group (182) was used instead of a triphenylphosphonium group as the program only handles up to 30 atoms. The P-H bond length is taken from ref.171.

Previous work by Pople's group[168] suggests that the most stable conformation of atoms in the 1′, 1′, 1′ trimethylammonio 2′-phenylacylimide ylide (159), is that which places the plane through C(7) - C(8) - C(1) at 90° to the plane through the benzene ring. Thus we have used this conformation, employing STD geometry, for the tolyl moiety and the geometry of the O = C - N - $N(H_3)$ group as in (181)[167], except for the angles C(1) - C(8) - C(7) and C(8) - C(7) - N(2) which were

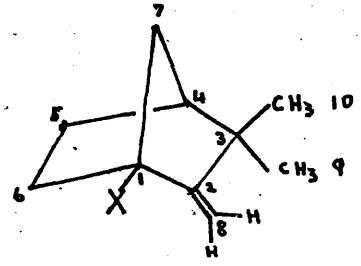
assumed to be 115° and C(8) - C(7) - O was assumed to be 122.5°. C(4), C(1), C(8), C(7), N(2), N(1) were all assumed to lie in a common plane.



X = H : 25 , X = OH : 28 , X = come : 31

$X = CH_3$: 26 , X = COOH : 29 , X = Cl : 32 , $X = NH_2$: 34

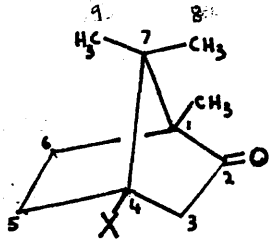
$X = CH_2OH$: 27 , $X = CO_2CH_3$: 30 , $X = NO_2$: 33



X = H : 35 , X = OH : 38 , $X = CO_2H$: 41

$X = CH_3$: 36 , X = Cl : 39 , $X = CO.NH_2$: 42 ; $X = NO_2$: 44

$X = NH_2$: 37 , $X = CH_2OH$: 40 , $X = CO_2CH_3$: 43



X = H : 45 , X = OH : 48 , X = Cl : 51 , $X = CO_2CH_3$: 54

$X = CH_3$: 46 , X = COOH : 49 , X = Br : 52 , $X = COCH_3$: 55

$X = NH_2$: 47 , $X = CO.NH_2$: 50 , $X = NO_2$: 53

DISCUSSION

^{13}C CHEMICAL SHIFTS OF 4-SUBSTITUTED TRICYCLENES[172]

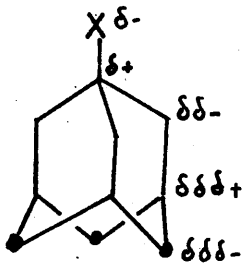
The conformational rigidity of bridged bicyclic systems allows certain aspects of the transmission of substituent effects in aliphatic derivatives, which are not observable in acyclic or monocyclic systems, to be investigated. Quantitative estimation of substituent effects in these systems is not possible owing to the presence of considerable ring strain.[84] However, important trends are discernible through correlation of the shift changes in one system with (i) the shifts observed in related systems (ii) parameters which measure the inductive and field effects of substituents (Table 1).

We have investigated the effect of a wide range of bridgehead, C(4), substituents on the magnitudes of the chemical shifts of 4-substituted tricyclene derivatives (25) - (34). Tricyclene derivatives are more synthetically accessible than those of nortricyclene, and the presence of γ and δ exocyclic methyl groups C(8), C(9) and C(10) provided an opportunity to study substituent effects on the magnitudes of the ^{13}C chemical shifts of primary carbons in this system.

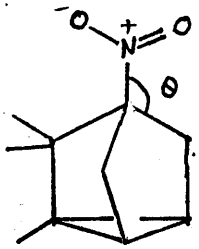
The ^{13}C n.m.r. spectrum of nortricyclene (10) and several methylated nortricyclenes have been reported.[94] Nortricyclene possesses C_{3V} symmetry and here only three signals are observed; C(1), C(2), C(6) at 10.2 p.p.m. from TMS, C(3), C(5), C(7) at 33.5 p.p.m. and C(4) at 30.0 p.p.m. Tricyclene (25), which possesses a symmetry plane passing through C(1), C(4), C(7) and C(10), is characterised by seven absorptions.

The ^{13}C chemical shifts of tricyclene derivatives (25) - (34) are given in Table (13), the corresponding substituent induced chemical shift increments are given in Table (14) and the ^{13}C chemical shifts of three 1-substituted bicyclo [2.2.2.] octane derivatives which supplement existing values are given in Table (15).

The assignment of ^{13}C absorptions in 4-substituted tricyclene (25) - (34) is accomplished by the use of proton



(56)



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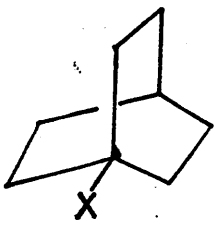
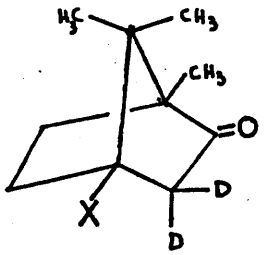


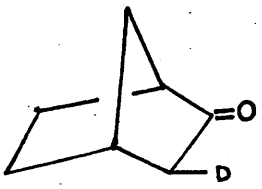
X=OH:57 , X= CO_2H : 59

X = CH_2OH: 58 , X= OCH_3 : 60

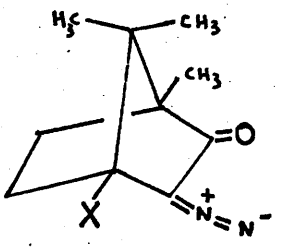


X= CH_3 : 63

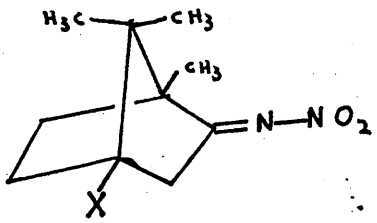
X = Cl : 64 X= NO_2 : 65



(66)



X= CH_3 : 74 , X= H : 75



X = H : 67 X = NO_2 : 69

X = COOH : 71

X = Me : 68 X = Cl : 70

off-resonance decoupled spectra. High field shifts which absorb at 9.4 - 12.2 p.p.m. and give quartets in the off-resonance spectra are attributed to C(10). The absorptions in the range 17.3 - 19.4 p.p.m. and are more intense than those for C(10) are assigned to C(8), C(9). Secondary C(3), C(5) and tertiary cyclopropane carbons C(2), C(6) are unambiguously assigned. There are three types of quaternary carbon C(1), C(4), C(7); C(1) absorbs in the range 26.3 - 29.8 p.p.m., C(7) in the range 43.05 - 47.7 p.p.m. while those for C(4) resonate over a wide range and were assigned by comparison with other similarly substituted compounds.

The absorptions of the α-carbons, C(4), in compounds (25) - (34) occur at consistently lower field than those of the corresponding 1-substituted adamantane (56) derivatives,[91] probably due to the presence of a gem dimethyl group on C(7) in the tricyclene derivatives. This point is illustrated by comparison of the C(4) chemical shifts of nortricyclene[94], 29.9 p.p.m., and tricyclene, 41.8 p.p.m.

The bridgehead carbon C(4) in tricyclene is located over the centre of a fused cyclopropane ring. Estimation of the diamagnetic anisotropy effect of the cyclopropane ring on the C(4) chemical shift of nortricyclene[94] using an R^{-3} dependence only accounts for 1 p.p.m. of the observed chemical shift difference (7.4 p.p.m.) between C(4) in nortricyclene and norbornane and the closer non-bonded separation of C(4) and C(1), C(2) and C(6) in former case has been suggested as being the source of this shift difference.

As is found in the adamantane derivatives[91] the chemical shifts of the α carbon in tricyclene (25) - (34) show a good linear relationship ($r = 0.988$) with electronegativity parameter, E_R; increasing electronegativity of the substituent causes low field shifts. However, the correlation between the α-carbon chemical shifts of tricyclenes (25) - (34) and those of the corresponding adamantane derivatives is less exact than that found between the adamantane α-shifts and those of the quaternary carbon of t-butyl derivatives.[91] The reason for this difference is possibly associated with the

presence of a β-gem dimethyl group in tricyclene or the decrease in the magnitude of the C(β) - C(α) - C(β) angles in tricyclene with respect to the other systems.

The α-carbon ^{13}C chemical shift increments of 4-tricyclyl derivatives and three related systems are given in Table (16). Comparison of these values shows that the largest low field shifts are found for bicyclo [2.2.2.] octyl derivatives and are of the same order of magnitude as those found for the t-butyl derivatives. 4-substituted tricyclenes and 1-substituted adamantanes have a considerably smaller α-effect than the other two series and the α-substituent increments of tricyclenes are generally smaller than those of adamantanes by ca. 1 p.p.m. However, for the chloro and nitro derivatives of the two latter series, larger deviations between respective chemical shift increments are observed.

The low field C(4) chlorine induced chemical shift increment in (32), 27.7 p.p.m., compares favourably with that found in three 4-substituted nortricyclonium ions in which the C(4) chlorine induced chemical shift was found to be 24.1 p.p.m.[173]

In the 4-substituted tricyclenes (25) - (34) there are two types of carbon atom which are β to the substituent, the secondary carbons C(3), C(5) and the quaternary carbon C(7). β-carbon chemical shift increments have not been successfully related to any single substituent parameter owing to the complex nature of substituent effects which influence the chemical shifts of this position.

It has been shown that adequate correlation exists between the chemical shifts of C(2) in 1-substituted adamantanes[91], the methyl carbons of 1-substituted cyclohexanes.[76] However, the correlation of C(3), C(5) shifts in 4-substituted tricyclenes with C(2) shifts in adamantanes (56) is considerably less satisfactory ($r = 0.870$).

Using the division of substituents introduced by Lippmaa's group,[91] it is found that Class I substituents containing no more than one atom heavier than hydrogen, cause larger paramagnetic shifts of the secondary β-carbons C(3), C(5) in tricyclenes (25) - (34) than is found for those

containing more than one atom heavier than hydrogen (Class II). This parallels the trend found for the adamantane derivatives. Table (17) gives the β-carbon chemical shifts for four structural types together with the derived low field β-shifts.

Inspection of the β-carbon chemical shift increments for Class II substituents in Table (17) indicates that tricyclene derivatives have consistently larger paramagnetic shift increments than those of the other series. From the results for the adamantane derivatives it was suggested that 1, 4 interactions were an important factor in the β-shift increments of Class II substituents.

4-substituted tricyclenes may be conceptually derived from bridgehead substituted adamantanes by (i) deletion of the marked carbons in (56) and replacement by bridgehead - bridgehead bonds, (ii) introduction of three methyl groups.

The effect of this process is to introduce into (nor)-tricyclene significant strain and distortion of bond angles.[166] In the case of 1-nitroadamantane it is calculated, with the aid of standard nitro parameters,[171] that in the eclipsed conformation with an O(1) - N - C(1) - C(2) dihedral angle equal to 0°, the C(1)---C(2) non bonded distance is 2.62 Å. Similarly for 4-nitrotricyclene (33), taking $\theta = 115.3^{\circ}$ the C(1)---C(3) non bonded distance in the conformation with dihedral angle O(1) - N - C(4) - C(3) = 0° is 2.74 Å.

In conformations in which the above dihedral angles depart from 0° to the same extent, the O(1)---C(3) distance in 4-nitrotricyclene will always be greater than the corresponding O(1)---C(2) distance in 1-nitroadamantane. The diamagnetic screening of C(2) in 1-nitroadamantane by the oxygen atoms of the nitro group, therefore, has to act over a shorter distance as compared with the same effect on C(3) of (33); accordingly the contribution of this component to the substituent induced chemical shift increment is greater in the adamantanes and the greater downfield shift for C(3) in 4-nitrotricyclene with respect to C(2) in 1-nitroadamantane is therefore rationalised.

Similar conclusions are in order for the other Class II bridgehead substituents. Analogous geometric considerations of the other systems in Table (17) are in accord with the

results above. However, the t-butyl group being acyclic and possessing primary β-carbons is not strictly comparable with the other systems.

From an investigation of the ^{13}C chemical shifts of exo and endo 2-substituted norbornanes (9)[84] it is also discernible that smaller substituent chemical shift increments obtain for the β-carbons C(3) for Class II substituents irrespective of whether the substituent is exo or endo. The chemical shift increments for C(1) in (9) show a similar result although the distinction between Class I and II substituents is less marked.

Substituent induced chemical shift increments for C(7) in tricyclenes (25) - (34) indicates that shifts to lower field are observed for this carbon compared to those of C(3), C(5), with Class I substituents. This is in agreement with the result previously suggested with reference to norbornyl systems[84] i.e. that the β-shift depends on the degree of substitution at the α and β-carbons but is essentially independent of other changes in the system. For Class II substituents C(7) shifts are on average of the same magnitude as the corresponding C(3), C(5) values.

Comparison of the chemical shifts of 1, 7-dimethyl-norbornane, and bornane[89] indicates that the introduction of a methyl group at C(7) in 1, 7-dimethylnorbornane to give bornane produces different low field changes in chemical shift at positions β to the incoming methyl group in bornane; for the methyl groups C(8), C(9) a low field shift of 9.2 p.p.m. is observed, for C(4) and C(1), the shift changes are 4.4 p.p.m. and 2.2 p.p.m. respectively. Therefore, for the particular β-carbons the low field shifts are in the order primary > tertiary > quaternary.

For the addition of an exo methyl group at C(2) of endo 2-methyl norbornane to give 2, 2 -dimethyl norbornane,[89] the shift differences at the endo-methyl, C(3), and C(1) are 9.8 p.p.m., 8.3 p.p.m. and 6.0 p.p.m. respectively, giving an order of low field β- shifts primary > secondary > tertiary. These results suggest that the magnitude of low field shift changes at a particular β-carbon follows the order primary > secondary > tertiary > quaternary.

These conclusions are supported by comparison of literature values of the chemical shifts in variously methyl and hydroxyl substituted bicyclo [2.2.1.] heptyl derivatives,[89] except in the following cases

(i) The ethano bridge, C(3), shift brought about by introduction of an exo - 2 - hydroxy substituent into endo - 2 - methyl norbornane is now larger than the methyl β-shift.

(ii) The effect of C(3) β-substitution is always greater than that for C(1) except in those cases which result in vicinal exo-exo or endo-endo methyl-methyl or methyl-hydroxy groups where steric compression effects probably cause the diminished C(3) β-shift values. A further point of interest is that both ethano bridge and bridgehead β-effects are greater for introduction of an exo as opposed to an endo hydroxy or methyl.

As a result of the rigid cage like structure of adamantane 1, 4 interactions between the substituent and the γ-ring carbons are greatly reduced relative to those found in cyclic and acyclic systems. This should result in a negligible steric component in the substituent chemical shift (S.C.S.) increments for γ-carbons in 1-substituted adamantanes and thus moderate correlation is obtained between the γ-chemical shifts of compounds with Class I substituents and the linear free energy parameter, σ^*.[91]

The 'tied-back' geometry of the tricyclo [2.2.1.$0^{2.6}$] heptane ring skeleton militates against direct 1, 4 interactions to a greater extent than for adamantane and here a correlation of the shift increments of C(2), C(6) in tricyclenes and E_R (r = 0.958) for the whole range of substituents is observed. The slope of this relationship is negative i.e. more strongly electron withdrawing substituents bring about high field shifts. This is opposite to the S.C.S. trend found for γ-carbons in 1-substituted adamantanes but similar to those found by us for the C(6) S.C.S. of 4-substituted camphors (45) - (55) and for the C(6) S.C.S. of exo - 2 - substituted norbornanes.[84] Thus the possibility of a diamagnetic effect arising solely from the presence of a fused cyclopropyl ring in the tricyclene system is unlikely.

For adamantanes it was suggested that the existence of charge alternation within a cyclic framework permitted rationalisation of the low field γ-shifts[91] and high field δ-shifts observed in this series and the high field δ-shifts observed in monosubstituted cyclohexanes.[76] Thus the high field γ-shifts of C(2),C(6) in tricyclene, which have a similar range as the high field δ-shifts in adamantanes and cyclohexanes (ca. 2 p.p.m.), could also be the result of charge alternation in the tricyclic framework.

The model of charge alternation in the adamantyl framework (56) is supported by evidence from C.N.D.O/2 charge density calculations, Table (18). Consideration of S.C.S. trends for adamantyl derivatives involving Class I substituents, in which discernible inductive trends exist for C(1), C(3) and C(4) and the shifts for these carbons are to low field, low field and high field respectively, suggests on an alternating inductive model high field shifts should result at the β-carbon C(2). However, for all the systems in Table (17) low field shifts are observed at the β-carbon with every substituent. The major factors which are expected to cause a perturbation from this idealised inductive behaviour are steric or stereo-electronic effects involving through space field interactions. These interactions would have to be downfield in nature and be of considerable magnitude. 1, 4 steric effects are known to be diamagnetic while 1, 5 effects have recently been shown to lead to downfield shifts.[82, 174] Batchelor has suggested that 1, 5 steric effects are caused by a second order field effect,[83] which can operate over short distances and, therefore, the β-carbon could be influenced by this (downfield) effect.

As a measure of this effect at the β-position, the model used by us to rationalise high field shift effects at the β-position by Class II substituents should be applicable to the low field shifts of Class I substituents. Using values from Table (17) respective S.C.S. values of hydroxy, chloro and amino derivatives of adamantane and tricyclene are seen to be in agreement with the hypothesis that a decrease in the substituent---β-carbon distance in moving from tricyclene to

adamantane causes larger downfield shifts as there is a greater interaction between the substituent and ring carbon; however the methyl group produces similar β-shifts in both systems. These results are broadly applicable to all the systems in Table (17).

On this basis, the substituent effect of a Class II substituent on a β-carbon would consist of two components, a large downfield 1, 3 interaction between the β-carbon and the substituent atom α to the ring, modulated by a 1, 4 diamagnetic interaction of the second heavy atom with C(β) resulting in smaller downfield β-shifts for Class II substituents as compared to Class I substituents.

Examination of C.N.D.O/2 charge densities for the α-carbon of bridgehead substituted adamantanes, Table (18), shows that there is some correlation with the ^{13}C chemical shifts for Class I substituents, but for this relationship to be valid for all substituents the α-carbons in Class II substituted compounds should resonate further upfield than is observed. These deviations are consistent with the concept of charge alternation as those substituents with an electronegative atom i.e. N, O two places removed from the ring, (Class II substituents), induce higher electron density at the bridgehead carbon than the comparable substituent containing only one electronegative atom e.g. compare NO_2 and NH_2 derivatives Table (18).

Since the pattern of ground state charge densities on the α carbon, $q_{V\alpha}$, does not explain the full range of S.C.S. values at C(2) some factor not contributing to $q_{V\alpha}$ either modifies or replaces $q_{V\alpha}$ as the principle contribution to the total chemical shift at this carbon.

There are two possibilities as to the source of this effect. Firstly, changes in the electronic population between the substituent and C(α) caused by the differential polarising capabilities of the substituent (X).[95] Inspection of the C(α)- X bond orders for adamantane derivatives shows no discernible trend.

Secondly, changes in the mean excitation energies, ΔE, of the α carbon. This type of rationalisation has already been advanced to explain similar anomalies in the relationship of C(α) shifts of mono-substituted benzenes

to q_{V_α}.[103] The substituent trend for q_{V_α} in the benzenes and adamantanes shows a reasonable linear relationship which is not surprising as σ inductive effects should control the value of q_{V_α} in both cases. 'Discrepancies' in the ipso carbon chemical shifts of nitrobenzene and benzaldehyde are attributed to the presence of low lying $\pi \longrightarrow \pi^*$ excited states which lower ΔE, thereby causing a downfield shift from that predicted by charge densities.

The mixing of ground and excited states via orbital distortion, the second order field affect, can effect the value of ΔE. This effect has been quite successful at predicting certain chemical shift trends in cyclobutanes[175] and the ortho chemical shifts[176,177] in aromatic systems. There are two measures of this effect;[175] both are of a semi-empirical nature.

Firstly, Q values[175] : $Q = \frac{PI}{r^3}$

where for system substituted with a substituent (X)

P = the polarisability of the C - X bond
I = the first ionisation potential
r = the C - X bond length.

Secondly, the time averaged square of the electric field $\langle E^2 \rangle$[175] : $\langle E^2 \rangle = \frac{PI}{r^6}$

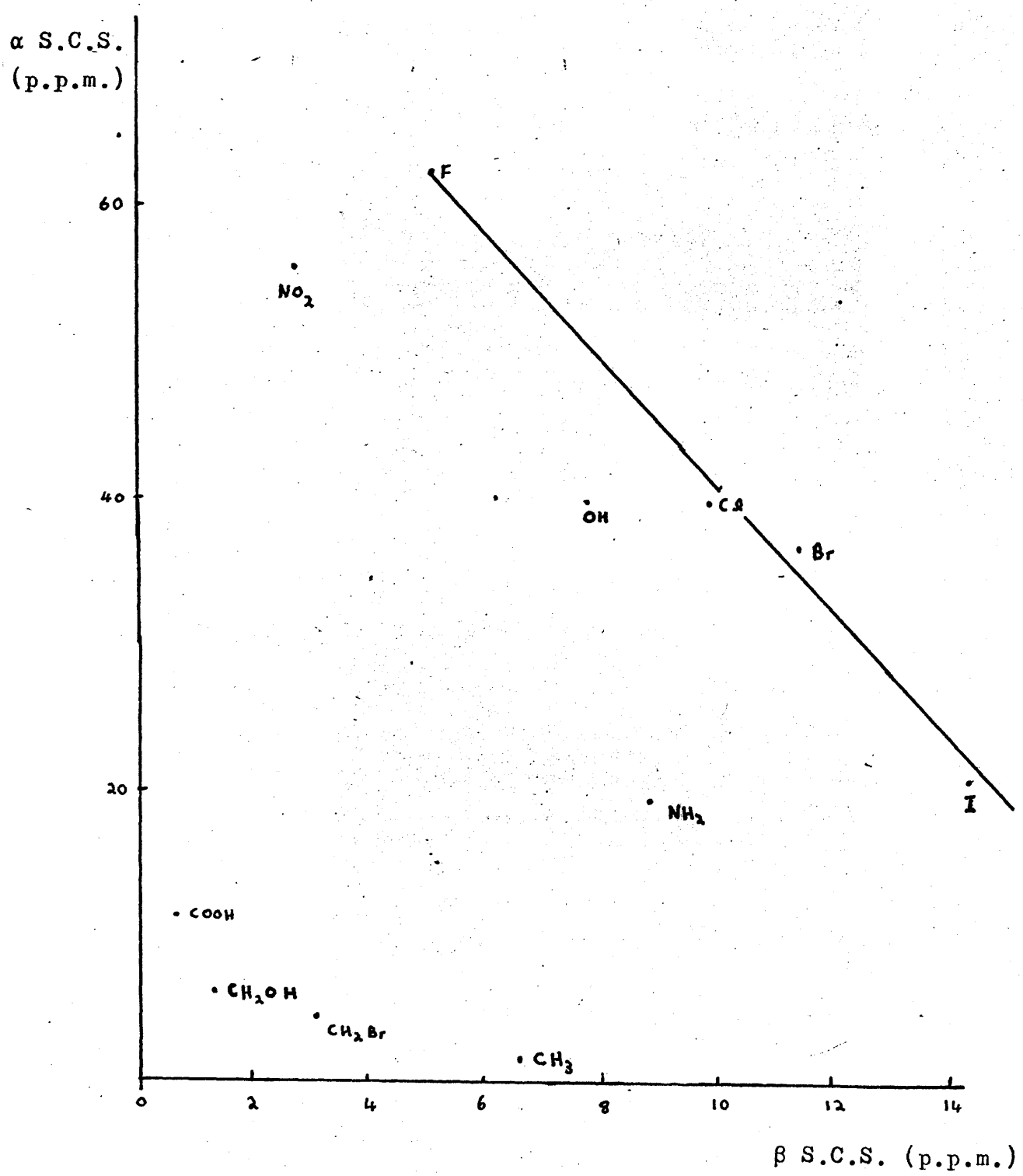
where r, in this case, measures the distance from the nucleus being considered to the substituent (X).

$\langle E^2 \rangle$ values are only available for monovalent substituents but Q values have been estimated for most common substituents. It is found that the largest Q values and hence second order field effects are found for the NO_2 and COOH substituents.[177] Second order field effects cause downfield shifts and previously changes in Q values have rationalised α-chemical shift changes of up to 80 p.p.m. in aromatic systems.[176] This is of sufficient magnitude to rationalise all the deviations from a linear chemical shift-charge density relationship at the α carbon.

Second order field effects find wider application in rationalising the shifts observed at β carbon atoms. Emsley et al[175] have shown that second order field effects as measured by $\langle E^2 \rangle$ predict the sequence of chemical shifts

fig. 7

Adamantane: α-S.C.S. vs β-S.C.S.



for molecules of the type CH_3 - C X,Y,Z where X, Y, Z are monovalent atoms e.g. halogens.

The ground state charge density at the β-carbon, q_β, is found to be inversely proportional to q_α and for secondary β-carbons no relationship is found between S.C.S. values and q_β. Interestingly, S.C.S. values of the quaternary β carbons C(7) in 4-substituted tricyclenes (25) - (34) give reasonable correlation with the C(7) electron density (r = 0.932). The electron densities of tricyclene derivatives are given in Table (19). Further, the difference in S.C.S. values between C(7) and C(3) or C(5) in both tricyclenes and 4-substituted camphors (see next section) are linearly related (r = 0.996). Since quaternary carbons have no contribution from the uniform field effect, the shift differences should measure the uniform field effect[178] of the substituent on the secondary β-carbon.

At positions more distant from the substituent than the β-carbon a correlation with ground state charge densities is more likely, as second order effects based on a distance dependence $\frac{1}{r^3}$ or $\frac{1}{r^6}$ are now expected to be negligible. Through-the-bonds inductive effects are expected to be fairly small as these effects also have a steep distance dependent attenuation factor,[179] and hence (uniform) field effects are likely to be the main contributory factor to S.C.S. at carbon atoms distant from the substituent in aliphatic systems.

We have already noted that the β- S.C.S. trend shows no correlation with any substituent parameter or the calculated charge density on the β-carbon. Certain trends are observable for β- S.C.S. values and we have found that by plotting these shifts against the respective α- shifts, as these follow a recognisable inductive order, certain substituent effects are observable. This is illustrated for the α and β-shifts of 1-substituted adamantanes in fig.(7) but is general for most aliphatic series.

Inspection of the graph in fig.(7) indicates that for Class I substituents β-effects are composed of three types; halogens; F, NH_2, OH; CH_3. Results from fig.(7) also imply that the postulated downfield 1, 3 effects are greatest

for the heavy halogens and F, OH, NH_2 are next in magnitude but those for CH_3 are anomalously small possibly because this substituent possesses no lone pairs.

Evidence that the β-effect for Class II substituents is composed of two components is provided by the results in fig.(7) for CH_3, CH_2-OH, and COOH substituents. These are linearly related suggesting that the 1, 3 effect of the methyl group is modulated by the 1, 4 effect of second heavy atoms. The results for these three compounds also indicate that greater 1, 4 upfield shifts are obtained for substituents with two heavy atoms β to the ring (COOH) than those with only one β- heavy atom(CH_2-OH)

The dissociation constants of 1-substituted bicyclo [2.2.2.] octyl carboxylic acids have been shown to be primarily controlled by the field effect of the substituent[179] and hence the σ_I scale derived from these dissociation constants should measure the field effects of substituents.

The high field δ-shifts of 1-substituted adamantanes correlate well with σ^*,[91] which is derived from σ_I, suggesting that they are due to the field effect of the substituent. These chemical shifts also show a poor linear relationship with the calculated charge density on the δ-carbon, q_δ, (Table 18) ($r = 0.88$). This result indicates that these field effects do not contribute to q_δ or that the method of calculation is not sensitive to field effects.

Further evidence that high field δ-shifts in adamantane[91] and cyclohexane[76] are the result of field effects can be obtained by comparison of the published results of the protonation shifts of pentylamine[178] with those for cyclohexylamine[76] and 1-adamantylamine.[91]

Table 20 shows that the trends for α, β and γ protonation shifts of the acyclic system are followed by the two cyclic systems. However, for the two cyclic systems the δ-protonation shifts are found further upfield than those of the γ-carbons.

Using the analysis outlined by Batchelor,[178] this result suggests that there is a larger uniform field contribution to the total chemical shift of δ-carbons in adamantane since for protonation shifts only the uniform field effect causes an upfield shift.

A possible rationalisation of these observations can be

obtained from an examination of a model of 1-aminoadamantane and pentylamine. There are three factors all of which suggest a larger uniform field effect for the δ- carbon in an adamantyl system.

(i) There is an increase in the substituent---δ-carbon distance in going from 1-aminoadamantane to pentylamine

(ii) The polarisability tensor A_Z (C) is greater for a secondary carbon than a primary carbon.[178]

(iii) The uniform field chemical shift is proportional to the cosine of angle between the electric field and A_Z (C). This is greater for the adamantane δ- carbon than the pentyl δ- carbon assuming the latter system to be in the extended planar conformation.

Hence protonation shifts can provide important information on the origin of high field shifts and the observed charge alternation observed in C.N.D.O. calculations in cyclic systems.

Charge density differences do not provide a rationalisation for the difference in S.C.S. trends for the secondary γ- carbons C(2), C(6) and the quaternary γ-carbon C(1) in tricyclenes (25) - (34) as charge density trends are the same for both carbons Table (19). The chemical shifts of C(2), C(6) correlate reasonably well with the charge densities (r = 0.926).

However, the sense of this correlation is contrary to that expected from the Karplus equation i.e. an increase in charge density at a given nucleus is expected to bring about a high field shift whereas the opposite effect obtains here. In addition, we note that C.N.D.O/2 calculations predict the same change in charge densities for C(1) and C(2), C(6) in tricyclenes (25) - (34) with change in substituent but their ^{13}C S.C.S. trends are completely different.

For the S.C.S. of the γ- quaternary carbon atoms in all the systems investigated in this study, 4-substituted tricyclenes and camphors together with 1-substituted camphenes, we did not observe correlation with any substituent parameter or calculated charge density.

Examination of the chemical shifts of exo-methyl groups C(8), C(9) and C(10) in tricyclenes (25) - (34) indicates that

the high field γ'-shifts for C(8), C(9) correlate with the corresponding low field δ'-shifts of C(10) with the largest values exhibited by Class I substituents (r = 0.970); γ' and δ' imply that these carbons are γ and δ to the substituent but are not ring carbons.

If it is assumed that steric effects make an unimportant contribution to the overall shielding of C(8), C(9) and C(10) then charge alternation could provide an attractive explanation of the chemical shift trends observed. The 1, 4 interactions between a substituent and a γ-ring carbon have been suggested to measure steric or stereo-electronic effects of the substituent[84] and increasing 1, 4 interactions produce high field shifts. The "tied back" geometry of the tricyclic ring system has earlier been suggested to militate against this type of interaction affecting C(2), C(6) and for the latter carbons lower field shifts are found than in the case of C(8), C(9) for Class I substituents. This would suggest the presence of 1, 4 steric interactions in the chemical shift of C(8), C(9). Further Class II substituents produce, in general, larger downfield shifts at C(8), C(9) than at C(2), C(6). This is consistent with more efficient 1, 5 interactions between the second heavy atom and the carbon in the former case.

The chemical shift of C(10) is unlikely to be influenced by steric effects and inductive effects acting over four bonds would not be expected to cause S.C.S. of up to 3 p.p.m.; C(4) in 1-substituted n-butyl groups show no substituent effects.[96]

Earlier in this section the importance of field effects in determining the chemical shifts of δ-carbons in adamantanes has been alluded to. The large magnitude of the δ S.C.S. of C(10) in tricyclenes (25) - (34) suggests that field effects, which have smaller fall-off factors than inductive effects, should strongly influence the magnitude of these shifts.

The C.N.D.O/2 nuclear charge densities of C(8), C(9) and C(10) in the tricyclene derivatives do not correlate with their respective chemical shifts. However, the nuclear charge densities of C(8), C(9) show a linear relationship with those of C(10) (r = 0.962).

A rationalisation of these shift trends in terms of field effects is possible. C(8), C(9) in tricyclene are tied-back from the substituent relative to the expected position of such groups in an acyclic system. Thus it is possible that they experience diminished field gradient and second order field effects in this system[178] as compared to an acyclic system. The latter field effects would be expected to be negligible for C(10) hence it is possible that both C(8), C(9) and C(10) experience solely the uniform field effect of the substituent and this would account for the linearity of the two sets of shifts.

It is not possible to explain the downfield nature of the C(10) chemical shifts on the basis of field effects as they are understood at the present time. The protonation shifts of 4-aminotricyclene may, however, yield important information on the nature of field effects in these systems.

^{13}C CHEMICAL SHIFTS OF 1-SUBSTITUTED CAMPHENES[180]

The ^{13}C chemical shifts of 1-substituted camphene derivatives (35) - (44) are given in Table (21) and the corresponding substituent induced chemical shift increments are given in Table (22). 1-substituted camphene derivatives (35) - (44) have no symmetry characteristics and assignments of the ^{13}C absorptions to particular carbons are achieved by consideration of chemical shifts, together with their substituent dependence where a suitable analogy is available and also by off-resonance spectra.

The exocyclic methyl groups C(9), C(10) exhibit limited substituent dependence of chemical shift, such that no overlap is observed, and assignment is made throughout such that the endo C(9) methyl is at higher field than C(10). Assignment of the three secondary carbons C(5), C(6) and C(7) is achieved in a similar manner and partial support is provided by consideration of the off-resonance spectra where the exact triplet due to C(7) contrasts with the presence of additional structure in the triplets for C(5) and C(6).[181] The remaining carbons C(4), C(1), C(3) are assigned without ambiguity.

In relation to other bridgehead substituted bicyclic and tricyclic systems the substituent bearing carbon C(1) of the camphenes absorbs at lower field an account of the electron withdrawing character of the exocyclic double bond; however, the low field α-S.C.S. of camphenes (35) - (44) are of comparable magnitude to those of related systems and empirically correlate well with linear free energy parameter, E_R, ($r = 0.984$).

In the present study of 4-substituted tricyclenes (preceding chapter) the magnitude of high field shifts for Class II derivatives and low field shifts of Class I derivatives observed for the secondary β-carbons of this system were rationalised in terms of the distance between a given substituent atom and the β-carbon.

In the camphene system it is not possible to predict unequivocally the substituent---β-carbon distance because

of different steric interactions between the substituent and the β-methylene group which will cause the substituent---C(6), C(7) distance to vary for different substituents, even though the geometry of the fused ring system would not be expected to be perturbed by changes in substituent character.[182]

Certain trends are observed on inspection of the ^{13}C shifts of secondary β-carbons C(6) and C(7) in these camphenes. The downfield shifts for Class II substituents are smaller than those of Class I at C(6) and C(7); for Class II substituents C(7) absorbs at lower field than C(6). This shows that these bulky Class II substituents must all occupy similar conformations when they are bonded to camphene at C(1).

The Class I substituents do not produce a consistent trend in C(6) and C(7) shifts in that for three Class I substituents lower field shifts result at C(7) than C(6) whereas the chloro derivative (39) produces a marginally greater downfield shift at C(6). This result could possibly be an indication that Class I substituents do not all exhibit the same spacial relationship to C(6) and C(7).

The chemical shifts of the SP^2 hybridised β-ring carbons C(2) in camphene derivatives (35) - (44) show moderate correlation with linear free energy parameter, σ_I, ($r = 0.915$). The shifts in this case are such that increased electron withdrawing character of the substituent causes a shift to higher field. In contrast to the SP^3 hybridised carbons C(6) and C(7), C(2) β-shifts of camphenes (35) - (44) are independent of whether the bridgehead substituent is Class I or Class II. These results are consistent with an increased uniform field contribution, which is expected as the polarisability tensor for an <u>exo</u> methylene group is approximately three times as large as that for a secondary carbon.[178] Thus linear field effects make a significant contribution to the screening of C(2). However, the inexact correlation of the C(2) chemical shifts with σ_I suggests that second order field effects, which are thought to dominate the chemical shifts of secondary β-carbons, still have an influence on the shifts of this carbon atom.

A further point of interest occurs in respect of the C(2) β-shift in the hydroxymethyl derivative (40) where high

dilution i.r. spectral measurements indicate partial intramolcular hydrogen bonding is of the π····H-O type. No such hydrogen bonding is observed in the case of a hydroxy substituent (38) where an unfavourable geometry exists. We were unable to obtain evidence from the i.r. spectra of the carboxylic acid derivative (41) for the presence of intramolecular hydrogen bonding.

The upfield shift of C(2) in (40) contrasts with the low field shifts of ca. 7 p.p.m. observed for the carbonyl carbons of e.g. ortho-substituted acetophenones[183] where hydrogen bonding occurs with non-bonded electrons on oxygen. It is possible that in (40) a situation obtains where the high field β-shift of C(2) is a composite effect containing a low field component on account of hydrogen bonding although it is possible that at the higher concentrations and in the different solvent of the n.m.r. experiment the role of an intramolecularly hydrogen bonded component of (40) is minimised.

Reasonable correlation between C(2) chemical shifts in the camphenes and the β-carbon shifts of 1-substituted prop - 2 - enes[184] is obtained for the limited range of substituents which are common to both series, while the C(8) chemical shifts in camphenes show good correlation with the respective γ-carbon chemical shifts of 1-substituted prop - 2 - enes.

If we exclude (40) from a discussion of the S.C.S. of C(8), as the C(8) shift of (40) is influenced by the effect of intramolecular hydrogen bonding, then the substituents which caused high field shifts at C(2) cause low field shifts at C(8). However, no correlation with any substituent parameter can be found for the complete range of substituents.

For Class I substituents those substituents whichproduce the largest downfield shifts at C(2) produce the greatest upfield shifts at C(8) whereas Class II substituents tend to produce fairly constant C(8) S.C.S. values which do not specifically reflect the magnitude of their effect on C(2) shifts.

Charge alternation in C(2) and C(8) is a possible explanation of the effect of Class I substituents on the

chemical shifts of these carbons. These results parallel those for 1-substituted butadienes, in which the chemical shifts have been shown by C.N.D.O/2 calculations to follow the pattern of charge alternation in the butadiene molecule.[185]

^{13}C CHEMICAL SHIFTS OF 4-SUBSTITUTED CAMPHORS, CAMPHOR NITRIMINES AND THE ^{15}N CHEMICAL SHIFTS OF DIAZOALKANES.

The ^{13}C chemical shifts of 4-substituted camphors (45) - (55) are given in Table (23) and the corresponding substituent induced chemical shift increments are given in Table (24).

The assignment of absorptions in the ^{13}C n.m.r. spectra of camphor derivatives (45) - (55) are made in an analogous fashion to those of other bicyclic systems,[172,180] and are supported by proton decoupled off-resonance spectra, and the presence of additional fine structure in the off resonance signal for C(5), C(6) as compared to C(3) is in accord with the finding of Grutzner[181] in related systems. The observation that generally in camphors (45) - (55) C(4) absorbs 2 p.p.m. to low field of C(4) in the respective tricyclenes (25) - (34) and 3-5 p.p.m. to higher field than corresponding carbon C(1) in camphenes (35) - (44) aids the assignment of C(4) in (49) and (55) in the spectra of which three quaternary carbons occur within 10 p.p.m. of each other.

The response of α-shifts for C(4) and β-shifts for C(3), C(5) and C(7) to substituent variation in the series (45) - (55) closely parallels those of the corresponding carbons in 4-substituted tricyclenes. The smaller β-shifts for C(3) with respect to C(5) are probably not due to a differential 'γ-effect' shielding from C(8) and C(9) on account of ring distortion. This is indicated by similar respective C(3) and C(5) β-shifts observed in the particular case of (46) and 4-methylnorcamphor.[186]

The <u>syn</u> C(8) methyl carbons in (45) - (55) are taken to absorb at lower field than the <u>anti</u> C(9) methyl carbons in accord with precedent although for (45) - (55) γ-shifts of C(8) correlate only moderately (r = 0.923) with those of C(9). Further no correlation is apparent between high field C(8), C(9) shifts in camphors (45) - (55) with the low field C(10) shifts as is observed in 4-substituted tricyclenes (25) - (34).

Rough correlation is found between the C(8) chemical shifts of C(8) in the camphor series and those of the

corresponding tricyclene and likewise the S.C.S. of C(10) in the tricyclene and camphor series show an approximate linear relationship. The chemical shifts of the C(9) methyl carbon in the tricyclene and camphor series show an excellent linear relationship, with the upfield shifts in tricyclene being approximately half the magnitude of those in the camphor series.

The x-ray structure of 3-bromocamphor[165] does not indicate any difference in the positions of C(8), C(9) with respect to C(4), however the spatial relationship between C(9) and the substituent in (45) - (55) must be significantly different from C(8) to cause the difference in shift trends, whereas the spatial relationship between C(9) and the substituent in the tricyclene and camphor series should be similar in order that they show the same S.C.S. trend.

The geometrical relationship between the C(4) substituent and the carbonyl group is such as to minimise any direct interaction. Here electron withdrawing substituents cause shielding of the carbonyl carbon C(2) such that the high field γ-shifts show a reasonable empirical correlation (r = 0.965) with the linear free energy parameter, σ_I. It should be noted that the correlation of the C(2) carbons in camphors with σ_I is considerably better than that for the C(2) carbon of 1-substituted camphene derivatives, possibly as a result of the absence of a contribution from second order field effects to the total shielding of the γ-carbon in the former case.

The (low energy) $n \longrightarrow \pi^*$ transition has been identified with the mean excitation energy, ΔE, and this has successfully correlated chemical shift trends in carbonyl[131,132] and nitroso[187] compounds. The change in the $n \longrightarrow \pi^*$ transition energies in monocyclic ketones of varying ring size has rationalised the change in carbonyl carbon chemical shift in these systems;[132] hence this transition appears to contribute significantly to ΔE in this type of compound. Since $\lambda_{max.}$ and ε are essentially the same for representative examples (45) (48) (51) and (53) (see Experimental section) this $n \longrightarrow \pi^*$ transition does not, via ΔE, account for the C(2) chemical shift variation.

Evidence has already been presented (see page 79) for proposing an important uniform linear electric field

contribution to the high field chemical shifts of the δ-carbon in adamantane which show good correlation with σ^* or σ_I. The chemical shift trends for γ-carbons C(2), C(6) in camphors (45) - (46) exhibit features in keeping with a field effect contribution to the S.C.S. values. For both sets of shift values there is a tendency for the S.C.S. values to be shifted to high field as the electron withdrawing power of the substituent increases. This is particularly noticeable for the chemical shifts of C(2), and employing Batchelor's theory of electric field shifts,[178] C(2) is expected to be more affected by field effects than C(6) owing to the increased polarisability of a carbonyl group as compared to a $-CH_2$ group. Thus the correlation of C(2) with σ_I is better than that for C(6) and it is expected that for this latter carbon other mechanisms of substituent effects may contribute more significantly to its total shielding.

It is found that C.N.D.O/2 charge density cannot account for the trend in S.C.S. values at C(2) or C(6) and, indeed, the trend in charge densities tends to suggest that the substituents causing the highest field shifts cause the lowest electron density at C(2) and C(6) (Table 25) contrary to that predicted by the Karplus equation[15] for the paramagnetic shielding constant. This result is similar to that found in our study of the relationship of the C(2), C(6) S.C.S. in 4-substituted tricyclenes and their respective electron densities. It appears that either the C.N.D.O/2 method is not sensitive to field effects or the nuclear charge density as calculated by this method is not the effective charge density contributing to the total shielding of the nucleus.

In addition, we have prepared 3, 3-dideuterio derivatives (63), (64) and (65). Their ^{13}C spectra show significant, 0.6 - 0.9 p.p.m., high field shifts for C(3) with respect to the all protio analogues (Table 26); the vicinal C(4) SP^3 hybridised and C(2) SP^2 hybridised carbons are respectively shielded and deshielded. Long range coupling $^3J_{C(5)-C(4)-C(3)-D\underline{exo}}$ results in broadening of the C(5) absorption with respect to that of C(6), thereby confirming the assignment in these cases. The analogous coupling $^3J_{C(7)-C(4)-C(3)-D\underline{endo}}$ is not of sufficient magnitude to permit detectable broadening of the C(7) absorption. In (63), (64) and (65) the C(3)

signal appears as a quartet of greatly reduced intensity with a quintet splitting ($^1J_{C(3)-D_3\ \underline{exo}} \equiv {}^1J_{C(3)-D_3\ \underline{endo}}$) of ca. 20.0 Hz.

C(4) and C(5) both experience high field isotope shifts, that for C(4) is 0.13 p.p.m. while that for C(5), 0.08 p.p.m., is greater than experimental error. The isotope shifts were confirmed both from small expanded spectra incorporating, in effect, more closely spaced data points and also with solutions containing both protio and di-deuterio species where resolution of the appropriate signals was obtained.

Previously 3-exo - $[^2H_1]$ - camphor, 3-endo-$[^2H_1]$- camphor and 5-endo - 6 - exo dimethylnorcamphor - 3 - exo - $[^2H_1]$ have been prepared;[1,90,188] here 3-exo deuterium substitution causes broadening of the C(5) absorption whereas 3-endo deuterium broadens that of C(7), both effects being due to the respective $^3J_{C-C-C-D}$ which exhibits the expected dihedral angle dependence. In general, $J_{C-C-C-H} > J_{C-C-H}$ and $J_{C-H} \simeq 6.5\ J_{C-D}$.[188]

^{13}C isotope shifts brought about through replacement of hydrogen by deuterium are well established.[189-192] These shifts are such that a deuterium bearing carbon undergoes a high field shift;[189,192] carbons β to deuterium are shielded when SP^3 and deshielded when carbonyl.[190] In addition, the present work shows that in (64) and (65) a ^{13}C isotope shift which is small but real is experienced at C(5) but not at C(7); in (63) the isotope shift is now experienced at C(5) but not at either C(7) or C(11) in 4-methylcamphor - 3, 3 - $[^2H_2]$. The only observable isotope effect, is that between Dexo and C(5) where the dihedral angle Dexo - C(3) - C(5) is in the order of 180°.

This situation finds an approximate parallel in that the largest non-deuterium vicinal substituent effect on a coupling constant, $J_{H-C-C-H}$ occurs when the bond to the substituent and one of the C-H bonds is antiperiplanar[193,194] in addition the greatest nuclear shielding caused by a vicinal substituent occurs when that substituent is antiperiplanar.[195] More recently high field fluorine shifts brought about by vicinal deuteration have been observed in cyclohexane and norbornane systems; here also the greatest shifts are observed when the D(H) - C - C - F dihedral angle

is greatest.[196]

The present results for deuterium induced high field ^{13}C shifts of C(3), C(4), C(5) in (63), (64) and (65) are in agreement with an electric field model. Since the direction of all the shift effects is the same and the effect of the deuterium induced shielding attenuates with distance.[197]

Vicinal delocalisation of σ electrons, which has been suggested as a possible mechanism for this type of system, has a pronounced angular dependence. However, a dideuterio system does not give any discriminating information in order to provide evidence for the existence of this type of mechanism.[198]

The upfield shifts observed for C(3) and C(4) in this system are in agreement with the concept of hydrogen in a C-H bond being more electron withdrawing than deuterium in a C-D bond. In the related 2-substituted norbornyl derivatives (9) electron withdrawing substituents at C(2) bring about low field shifts at C(2) and C(3);[84] accordingly the upfield isotope shifts at C(3) and C(4) in (63), (64) and (65) brought about by dideuteration at C(3) is rationalised.

The factors affecting the chemical shifts of C(6) in 2-substituted norbornanes[84] are not totally clear; upfield shifts are noted for both exo and endo electron withdrawing substituents. For the exo case greater electron withdrawing character produces larger upfield shifts and, in the endo case, more pronounced steric interactions are predicted to cause upfield shifts. However, deuterium is less electronegative and has a smaller steric requirement than hydrogen and, on this basis, a downfield isotopic shift is expected at C(5) in the camphor series on dideuteration of C(3). As upfield shifts are observed, there would appear to be a difference in the mechanism of isotope shifts and shift changes involving larger electronic perturbations of the system.

We have also examined ^{13}C shifts of a series of 4-substituted camphornitrimines (67) - (71) which are reported in table (27). For particular carbons the response of chemical shift to substituent variation is very similar to

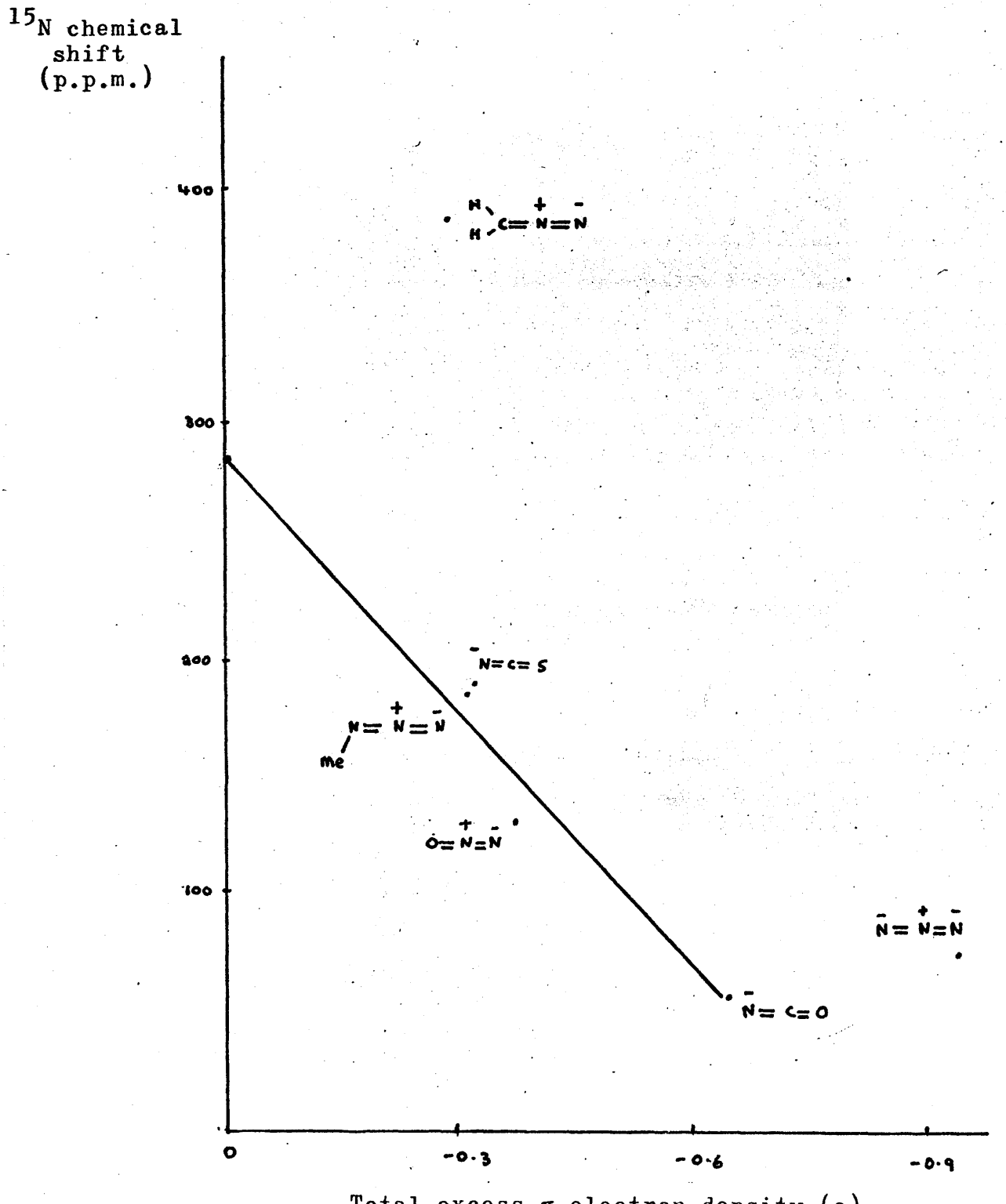
those of the corresponding camphors.

Predictably, largest shielding differences between the camphor and its nitrimine are observed in respect of C(2), C(3) and C(1). Thus C(2) in nitrimines (67) - (71) is shielded by 27.3 - 30.2 p.p.m. with respect to C(2) in the parent camphor. Additionally we find that C(9) in fluorenone nitrimine (73) absorbs at 163.5 p.p.m. as compared with 193.4 p.p.m. in fluorenone and in pinacolone nitrimine (72) C(3) absorbs at 181.4 p.p.m. in relation to the corresponding absorption at 210.7 p.p.m. in pinacolone. Elsewhere[199] it has been tentatively concluded that the imine bond in 4-substituted camphornitrimines is slightly less polar than the carbonyl bond in 4-substituted camphors on the basis of slightly smaller values of $^{4}J_{H_3\ \underline{exo}\text{-}H_5\underline{endo}}$ obtained for the nitrimines.

The nitrimine group in (67) - (71) is capable of geometric isomerism, although no evidence for this was found. Models indicate that a preferred configuration places the C(2) - C(3) bond <u>syn</u> to the N-N bond whereas in the alternate configuration an oxygen of the nitro group is situated close to the C(10) methyl group. In the latter situation, steric compression effects may be expected to cause a significant shift of C(10) with respect to the corresponding ketone. High field steric compression shifts are considered to apply unambiguously only to γ effects and recently syn-axial δ interactions have been shown to result in low field shifts. Since C(10) in (67) - (71) is deshielded by only <u>ca.</u> 1 p.p.m. from C(10) in the corresponding ketone, it is probable that in this series a common configuration obtains in which C(2) - C(3) and the N-N bonds are <u>syn</u>.

The ^{15}N chemical shifts of a number of diazoalkanes are given in table (28). The ^{15}N n.m.r. spectrum of (75) indicates that N(2) absorbs, with respect to external $\overset{+}{N}H_4$, at 383 p.p.m., a value close to that found for the terminal nitrogen of diazomethane (376 p.p.m.).[199] By analogy the low field absorption in the ^{15}N spectrum of 9-diazofluorene (76) is also assigned to the terminal nitrogen. In diazoalkanes the central nitrogen N(1) absorbs 23-40 p.p.m. downfield from the corresponding nitrogen in alkyl azides[200] (actually determined as a ^{14}N shift, the isotope effect for nitrogen being negligible) whereas the terminal nitrogen

fig. 8. The ^{15}N chemical shifts of terminal nitrogens, N(2) in a series of linear sixteen valence electron molecules v.s. Total excess π electron density.



N(2) in diazoalkanes is deshielded by 230 p.p.m. from N(2) in alkyl azides.

These characteristics are broadly shown by other molecules with a linear array of three multiply bonded "heavy" atoms. Examples which may be related to each other and the above include ^{13}C chemical shifts of allene,[136] ketene,[137] and nitrile oxides[202] and ^{15}N chemical shifts of the azide ion[200] and nitrous oxide.[203]

^{15}N shift variations in a series of linear sixteen valence electron molecules gave a linear correlation with π electron densities;[203] variations in the mean excitation energy, ΔE, were considered unimportant. Higher π electron density at the terminal carbon of ketene[136] has been proposed in order to rationalise the greater shielding with respect to the terminal carbon of allene, whereas the low field shift of the methylene carbons in diazoalkanes[137] with respect to ketene is attributed to reduction in σ electron density on account of the greater electronegativity of the N_2 group. Current C.N.D.O/2 calculations bear out the second of these two postulates, Table (29).

The ^{15}N chemical shifts for N(2) in the series above do not correlate linearly with the total π electron density on N(2) i.e. the sum of the P_y and P_z electron density on N(2), Table (29), figure (8); however, the wide range of ^{15}N shifts of the terminal nitrogens correlate fairly well with the lowest energy transition in each case (r = 0.961) Table (30).

The validity of equating the lowest energy transitions in these molecules with the average excitation energy, ΔE, is subject to doubt[21] but the large variation in the magnitude of the low energy transition for the compounds in Table (30) (300 n.m.) suggests that ΔE is not constant for the complete series.

We also note that the ^{15}N chemical shifts of compounds having approximately the same low energy transition e.g. those in Table (30) with $\lambda_{max.}$ 300 $\pm$ 30 n.m., show reasonable correlation with the total π electron density.

For the "central" nitrogen in these systems N(1) it is apparent from Table (28) that the range of ^{15}N chemical shifts for N(1) is much smaller than for N(2); by a factor of ca.4. Further, no correlation is found between the N(1) shifts and

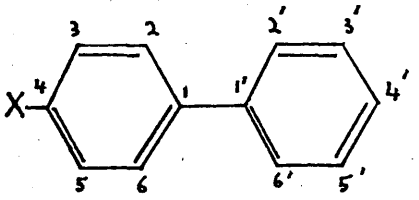
N(1) electron density or the lowest energy transition *per se*. However, the large changes in chemical shift observed for N(2) in these systems, together with smaller changes on the central atom N(1) is analogous to that found for the ^{13}C chemical shifts of C(7), C(8) in para-substituted styrenes (11)[114] where the change in π electron density at C(7) was too large in magnitude to explain the small range of chemical shifts observed. For the styrenes and related compounds we have attempted to rationalise the S.C.S. values in terms of changes in delocalisation of electron density on C(7) and for para-substituted acetophenones we have shown that changes in the $n \longrightarrow \pi^*$ transition energies can account for the small range of ^{13}C chemical shifts observed for C(7) in para-substituted acetophenones.

For the systems in Table (28) the changes in the molecule are occurring significantly nearer N(1) and N(2) than in C(7), C(8) in the para-substituted aromatic systems above. Hence it is impossible to analyse the results for these systems in more than a qualitative manner as changes in Δ E and π electron density are large and variable owing to the wide ranging changes around N(1) and N(2).

^{13}C N.M.R. SPECTRA OF ACETOPHENONE, 1′, 1′ DIMETHYL 2′-BENZOYLHYDRAZIDE AND 1′, 1′, 1′-TRIMETHYLAMMONIO 2′-BENZIMIDE DERIVATIVES.

Much of the interest in the factors affecting the magnitudes of ^{13}C n.m.r. shifts has centred on disubstituted aromatic systems. In such meta and para systems the two substituents are considered to be separated by too great a distance to exhibit mutual steric interactions, although here through space effects have been suggested as contributing to the overall shielding of carbon atoms.[114]

In recent years the wide availability of approximate molecular orbital calculations and the advent of D.S.P. treatments of S.C.S. values has aided the interpretation of the chemical shifts in terms of the relative contribution of various electronic mechanisms to the total chemical shift. This type of approach has been used for substituted styrenes (11),[114,115] phenylacetylenes (12),[116] phenylalkanes (13),[117] biphenyls (77),[204] benzonitriles[113] and benzoic acids.[109]



(77)

For a carbon nucleus changes in the paramagnetic contribution (σ_p) generally control the magnitude of the total chemical shift. In practical terms σ_p can be thought of in equation (1).[15]

$$\sigma_p = -\frac{1}{\Delta E} \cdot \frac{1}{\langle r^3 \rangle_{2p}} \cdot [Q_{AB}] \qquad (1)$$

The meaning of each of these terms has already been discussed on page 16.

In the ^{13}C studies listed above the nuclear charge density on each atom was suggested as the dominant factor controlling the magnitude of the chemical shifts in these systems via the $\langle r^{-3} \rangle_{2p}$ term and they assume that ΔE and Q_{AB} are constant.

The approximation that changes in the nuclear charge density obtained from C.N.D.O. or I.N.D.O. calculations reflect changes in the $\langle r^{-3} \rangle_{2p}$ term in equation (1), and hence changes in the chemical shift of the atom concerned, gave good correlation with the S.C.S. for some of the carbons in the systems listed above.[114,116]

However, changes in the nuclear charge densities could not account satisfactorily for changes in S.C.S. values of some of the carbon atoms in the systems above, notably C(7) in styrenes (11),[114] phenylacetylenes (12)[116] derivatives and the carboxyl carbon of para-substituted benzoic acids.[109]

The S.C.S. values of these carbon atoms give D.S.P. correlations which are difficult to explain in terms of electronic transfer. In order to provide a rationale for their results on the carboxyl carbon of para-substituted benzoic acids Niwa and Yamasuki[109] show that deviations of π electron donating derivatives from the regression line in a D.S.P. correlation are in the order and direction expected from an extra conjugative interaction between the two substituents and changes in the π bond order between the carboxyl carbon and the ring carbon to which it is bonded.

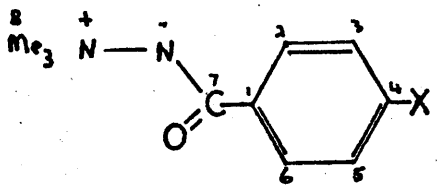
In a disubstituted aromatic system which involves one substituent containing a carbonyl carbon α to the ring, a change in the second substituent e.g. X in (11) will affect the distribution of electrons in the first substituent by several mechanisms.

(i) The mesomeric effect of the substituent will induce charges of alternating sign along the entire π system of the molecule, relative to the parent compound with hydrogen as the second substituent.

(ii) Changes in the π electron density of the system can also arise through π -polarisation[114,115] of the system not involving transfer of charge from the second substituent.

(iii) Steric interactions between the two substituents will affect the charge density distribution in both substituents for ortho-disubstituted derivatives.

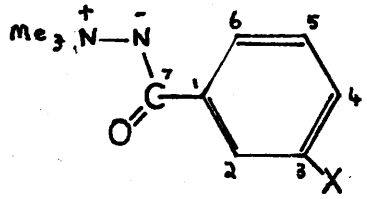
(iv) Changes of the type (i) can also cause complete polarisation of the molecule in para-disubstituted systems.



X = NMe_2 : 78 X = F : 81 X = CF_3 : 84 X = CN : 87

X = Me : 79 X = Cl : 82 X = NO_2 : 85 X = H : 88

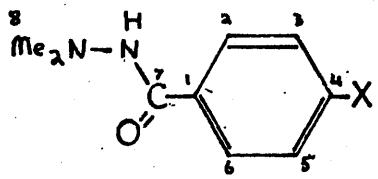
X = ome : 80 X = Br : 83 X = Ph : 86



X = Me : 89 X = Cl : 92 X = NO_2 : 95

X = ome : 90 X = Br : 93 X = CN : 96

X = F : 91 X = CF_3 : 94



X = Me : 97 X = Cl : 100 X = NO_2 : 103 X = H : 106

X = ome : 98 X = Br : 101 X = CN : 104

X = F : 99 X = CF_3 : 102 X = NMe_2 : 105

This conjugative interaction will be manifested in changes in the electronic population between atoms i.e. bond orders in addition to its effect on nuclear charge density.

In order to estimate the contribution of mechanisms (i), (ii), (iv) to the total shielding of carbon atoms in disubstituted aromatic systems we have measured the n.m.r. spectra of a series of (1) 1′, 1′, 1′ trimethylammonio 2′-benzimide ylides where the substituent is:

a) in the para position (78) - (88) see Table (31)
b) in the meta position (88) - (96) see Table (32)

(2) 1′, 1′ dimethyl 2′-benzoylhydrazides where the substituent is:

a) in the para position (96) - (106) see Table (33)
b) in the meta position (106) - (115) see Table (34)

(3) a) para-substituted acetophenones (116) - (125) Table (35)
b) meta-substituted acetophenones (125) - (133) Table (36)

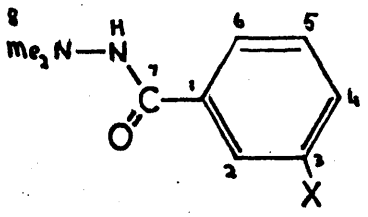
(4) para-substituted triphenylphosphonium ylides (134) - (141) and para substituted triphenylarsonium ylides (142) - (150) are given in Table (37)

The assignment of the spectra was straightforward; all non-benzene ring carbon chemical shifts could be assigned unambiguously. Ring carbon chemical shifts were assigned by comparison with the chemical shifts of mono-substituted benzenes. In addition the ring carbons of fluoro derivatives of the above systems could be distinguished by the presence of ^{13}C - F spin-spin coupling between each of the ring carbons and fluorine.

The geometry of the ylide (88) has been established by x-ray methods.[167] The results suggest that the O = C - N - moiety in (88) is at 17^{o} to the mean plane of the benzene ring.

Ab initio calculations on benzamide[168] suggest that its most stable conformation is that with the O = C - $N(H_2)$ plane at 30^{o} to the mean plane of the benzene ring, which agrees with the x-ray evidence which suggests the angle of twist is 26^{o}.[205]

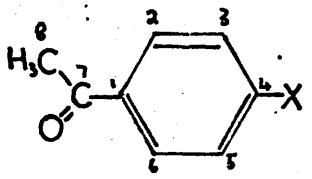
In contrast, an x-ray diffraction study of the geometry of p-nitroacetophenone[169] shows that the O = C - $C(H_3)$ moiety lies in the same plane as the benzene ring and here ab initio calculations suggest this is the most stable conformation.



X = Me : 107 X = Cl : 110 X = NO_2 : 113

X = OMe : 108 X = Br : 111 X = CN : 114

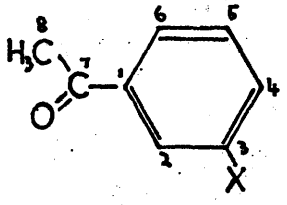
X = F : 109 X = CF_3 : 112 X = NMe_2 : 115



X = Me : 116 X = Cl : 119 X = NO_2 : 122 X = H : 125

X = OMe : 117 X = Br : 120 X = Ph : 123

X = F : 118 X = CF_3 : 121 X = NMe_2 : 124



X = Me : 126 X = Cl : 129 X = NO_2 : 132

X = OMe : 127 X = Br : 130 X = NMe_2 : 133

X = F : 128 X = CF_3 : 131

The non planarity of benzamide and the ylide (88) can be attributed to strong cross-conjugation between the nitrogen and oxygen attached to the carbonyl carbon reducing the π bond order between the carbonyl carbon and the benzene ring carbon C(1), and hence the presence of an unfavourable interaction between the ortho hydrogens and the lone pair of electrons or hydrogen on the nitrogen atom β to the ring causes the twisting observed.

Cross conjugation in the acetophenone will be negligible, hence there will be an increase in π bond order between the carbonyl carbon and C(1). The extra stability which the molecule acquires through this conjugative interaction apparently outweighs the decrease in stability caused by a steric interaction between the acetyl methyl hydrogen atoms and the hydrogens attached to C(2), C(6) of the ring.

The conformation of the benzhydrazide (106) can reasonably be expected to be similar to benzamide, and while the conformations of the phosphonium ylide (134) and the arsonium ylide (142) are unknown, it is possible that the arguments that applied to acetophenone also apply to (134) and (142) and indicate little cross conjugation in these two systems. Further evidence concerning this point will be discussed later.

The S.C.S. in the above systems were examined using three sets of substituent parameters;

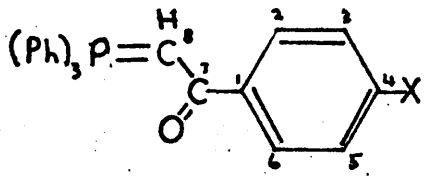
(i) single parameter treatment using σ_I, σ_R^o, σ_P, σ_M.
(ii) D.S.P. treatment with F and R.[48]
(iii) C.N.D.O/2 molecular orbital calculations.

The results of molecular orbital calculations on

(a) derivatives of the ylide (181) are given in Table (38)
(b) para-substituted styrenes (11) are given in Table (39)
(c) acetophenone derivatives are given in Table (40)
(d) para-substituted phosphonium ylide (182) are given in Table (41)
(e) para-substituted nitrobenzenes are given in Table (42)

<u>S.C.S. values for carbon atoms α to the benzene ring in para-substituted systems.</u>

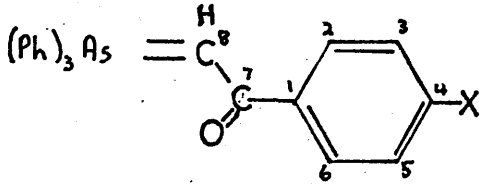
D.S.P. correlations for the C(7) S.C.S. in para-substituted ylides (78) - (88), hydrazides (97) - (106) acetophenones (116) - (125), phosphonium ylides (134) - (141)



X = H : 134 X = F : 137 X = CN : 140

X = Me : 135 X = Cl : 138 X = NO_2 : 141

X = ome : 136 X = Br : 139



X = H : 142 X = F : 145 X = CN : 148

X = Me : 143 X = Cl : 146 X = NO_2 : 149

X = ome : 144 X = Br : 147 X = Ph : 150

and arsonium ylides (142) - (150) are given in Table (43). The results for the ylides and hydrazides above indicate that superior correlation should be found between their C(7) S.C.S. values and Hammett constant σ_M than with the σ_P; S.C.S. of ylides (78) - (88) and hydrazides (97) - (106) both show good linear relationship with σ_M, r = 0.986, 0.970 respectively, since the %R value for σ_M is 22%.[48]

Correlations between σ_M and the ^{15}N S.C.S. of the nitro group in para-substituted nitrobenzenes[126] and the ^{13}C S.C.S. of C(1′) in the 4-substituted biphenyl system (77) have also been found.[204]

Interestingly, Pople[168] found that the C(1) - nitrogen π bond order in nitrobenzene and the C(1) - C(7) π bond order in benzamide were similar, 0.34, 0.35 respectively and our calculations show a comparable result for the ylide (88) and nitrobenzene, Tables (38), (42). In addition the angle between the planes of the biphenyl system was found to be about 45^{o}, probably due to low π bond order between the rings.[171]

These systems can all be visualised as containing the moiety Z = X - Y, where Y, Z are substituents which can bring about strong cross conjugation in the X, Y, Z moiety and reduce the π bond order between X and C(1) of the benzene ring.

Previously it has been suggested that the correlation of the ^{15}N chemical shifts of para-substituted nitrobenzenes[126] with σ_M and the lack of correlation of these S.C.S. values with the calculated π electron density provided evidence that the inductive effect of the substituent plays an important role in determining the magnitude of the ^{15}N chemical shifts of this system.

Accordingly, we have carried out C.N.D.O./2 molecular orbital calculations on para-substituted nitrobenzenes, Table (42); from these we find that, although the nitrogen σ charge density produces the correct trend in substituent effects, these results require that an increase in shielding is caused by a decrease in electron density, contrary to that predicted by equation (1). The σ electron density trends for C(7) of the meta and para-substituted ylides (78) - (88) and acetophenones, and para-substituted phosphonium ylides

also follow this 'σ_M' order; however the direction for the trend in all cases is contrary to that predicted by equation (1), see Tables (38), (40), (41).

For the para-substituted systems above it is apparent that changes in the π electron density on C(7) are much greater than changes in σ electron density but changes in the nuclear π electron densities do not account for the observed trends in the S.C.S. values.

Examination of the S.C.S. for C(7) in styrene[114] and the carbonyl carbon of acetophenones Table (35) indicates that upfield shifts relative to the parent compound are obtained for all derivatives in both series and the total chemical shift range is rather small (ca.2 p.p.m. in each case).

Reynolds[114] has suggested that the scaling factor of chemical shift to electron density should be of the order of 200 p.p.m./electron (e) for styrene derivatives. Using Reynolds results for the π charge densities of C(7) in styrene, this suggests that the chemical shift range should be ca. 4.3 p.p.m. instead of 1.93 p.p.m. as observed.

The nuclear charge density cannot be the only factor which is contributing to the value σ_p (see equation (1)) and, if ΔE and Q_{AB} are essentially constant for these systems, then nuclear charge density is not the only factor which is contributing to the value of $\langle r^{-3} \rangle_{2p}$. This extra contribution to $\langle r^{-3} \rangle_{2p}$ must reduce the effective electron density change at the carbon atom in question.

As stated earlier in this section changes in the π electron density at C(7) in these compounds are much greater in magnitude and opposite in direction to those of σ electron density, implying that changes in the π system induce changes in the σ system via the mechanism known as $\sigma - \pi$ polarisation.[206] Thus, consideration of electronic changes in the π system of the molecule should be able to account for the S.C.S. values at C(7). It has already been shown that changes in the C(1) - C(7) π bond order in para-substituted benzoic acids[109] explain deviations from a plot of C(7) S.C.S. values and C(7) π electron density. The most likely mechanism for this is that changes in the π bond order and changes in nuclear π electron density both contribute to an effective π electron density[207,208] which

is the true contribution of electronic changes in the system to $\langle r^{-3} \rangle_{2p}$.

Examination of the π bond orders in styrene, Table (39), shows that the increase in the C(1) - C(7) π bond order, which is found for all substituents, is greater in magnitude than the corresponding decrease in the C(7) - C(8) π bond order by a factor of ca. 2:1 ; changes in the C(7) - C(8) π bond order exactly mirror those of C(1) - C(7) π bond order. Hence changes in the bond order around C(7) are probably best measured by changes in the C(1) - C(7) π bond order as this should have the major effect on the effective electron density of C(7).

If changes in electron density, as calculated by approximate molecular orbital methods, are to be useful in accounting for S.C.S. values then changes in electron density should be within a range which gives a suitable chemical shift/electron density scaling factor and should predict the correct trend of substituent effects.

In order to obtain a suitable value for the p.p.m./e scaling factor we propose to divide the f coefficient of a D.S.P. correlation between F and R, and S.C.S. values for a given atom by the f coefficient of a D.S.P. correlation of F and R with the π electron density of that atom. Reynolds[114] has shown for styrenes that the f/f ratio for C(7) gave an acceptable p.p.m./e value (ca.200 p.p.m./e) even though the r/r value did not yield a suitable value.

Using the scaling factor it is then possible to work out the magnitude of the total change in electron density which can bring about the shift change observed. For styrenes the range of chemical shifts is 1.93 p.p.m.[114] which, using the accepted scaling factor, yields a change of 96×10^{-4}e.

We propose that this value (96×10^{-4}e) is composed of contributions from π nuclear electron density (q_Z) and π bond order changes (p_Z). For C(7) in the systems studied, bond order changes are probably measured most accurately by changes in the C(1) - C(7) π bond order.

By combining p_Z and q_Z values for a given carbon atom in a substituted system in an equation of the type,

$$\Delta = A\ q_Z \pm B\ p_Z \qquad (2)$$

where Δ are the S.C.S. increments,

and A and B are scaling factors for q_Z and p_Z

it should be possible to compare the relative importance of nuclear electron density changes and changes in bond order, which are a measure of delocalisation in the system, for a series of related compounds. For C(7) in the systems studied suitable values of A, B should generate a series of effective charge densities on C(7) which can account for the S.C.S. values observed for this atom.

In using equation (2) we have adopted the following sign convention, upfield shifts and an increase in electron density at an atom are negative. In order that this correlation is meaningful in predicting the effective change in electron density, at C(7), the values of A and B must lie between + and -1 in order that the sources of electron density changes can be accounted for i.e. for C(7) all electron density changes fall within the range $\pm$ C(7) nuclear π electron density $\pm$ C(1) - C(7) π bond order.

For the para-substituted ylides (78) - (88) comparison of the f values obtained from correlations of the C(7) S.C.S. values and the C(7) nuclear π electron densities with F and R yielded a scaling factor of 355 p.p.m./e. This implies an effective π electron density range of ca. 82 x 10^{-4}e. brings about the observed range of chemical shifts (2.9 p.p.m.)

The equation:-

$$\Delta = q_Z + 0.5\, p_Z$$

accounts for this range of chemical shifts and reproduces the trend in S.C.S. values fairly well (r = 0.948).

The S.C.S. values of styrenes which have a range of 1.93 p.p.m. can be considered to have been brought about by an electron density change of ca. 96 x 10^{-4}e using the accepted scaling factor of 200 p.p.m./e and the equation:-

$$\Delta = 0.5\, q_Z + p_Z$$

accounts for the S.C.S. range and trend, (r = 0.929)

The nitrobenzene system yields a similar result to the ylide system, here the equation:-

$$\Delta = q_Z + 0.8\, p_Z$$

accounts for the chemical shift trend (r = 0.998) and yields a scaling factor of 718 p.p.m./e .

For the para-substituted acetophenones, para-substituted phosphonium and arsonium ylides unsatisfactory D.S.P.

correlations between C(7) S.C.S. values and F and R are obtained, possibly because the R scale cannot account for the extremely large resonance interactions that occur between the carbonyl groups in these systems and π donating substituents in the para position, especially NMe_2. As can be seen from Table (43) if the NMe_2 group is not included then moderate correlation is obtained between the remaining S.C.S. values for C(7) in para-substituted acetophenones and F and R. Significantly the f coefficient only changes from -1.33 to -1.31, hence the approximation of obtaining a chemical shift/electron density scaling factor from f values is probably still valid. This process gives a scaling factor value of 288 p.p.m./e and an effective electron density range of 59×10^{-4} e .

For para-substituted acetophenones we find that the equation:-

$$\Delta = q_Z + 0.5\ p_Z$$

gives a reasonable fit for most substituents i.e. all except NMe_2, OMe and F. For these substituents, where an extra conjugative interaction is present with the acetyl group, the equation:-

$$\Delta = 0.25\ q_Z + p_Z$$

brings the effective electron densities into the correct range and correlation of the calculated effective electron densities and the S.C.S. values show a reasonable linear relationship ($r = 0.965$); however, this process does not account for the C(7) chemical shift of para-fluoroacetophenone.

For the phosphonium ylides (134) - (141) the f/f,S.C.S./electron density scaling factor for C(7) gives a value of 444 p.p.m./e and an electron density range of 66×10^{-4}e. The two equations used for para-substituted acetophenones above produce a linear correlation for all substituents ($r = 0.992$). Since the S.C.S. values of C(7) in the para-substituted phosphonium ylides correlate linearly with the C(7) S.C.S. values of the respective arsonium ylides (142) - (150) ($r = 0.993$), then the results above can be expected to apply in the latter series as well. The chemical shift electron density scaling factor for these series appears to be extremely high.

These results indicate in a qualitative manner the importance in considering changes in delocalisation in the system, via bond order, in accounting for the relationship of electron density to S.C.S. changes for a particular carbon.

Consideration of the relative importance of bond order changes to nuclear charge density changes for the systems above as calculated by equation (2) in terms of the ratio of scaling factors $\frac{B}{A}$ shows that the importance of delocalisation changes increases as follows; along the series ylide (88), nitrobenzenes < acetophenones, phosphonium and arsonium ylides < styrenes. Hence delocalisation increases in importance with increases in C(1) - C(7) π bond order, Tables (38) - (42).

The changes in delocalisation can also rationalise the %R values for D.S.P. correlations of F and R and C(7) S.C.S. values. From Table (44). it is apparent that correlation of C(7) π electron density values with F and R yields a fairly constant %R value (ca. 50%). The observed %R values for the S.C.S. of C(7) in these systems is much lower and for acetophenone it is negative since the extra conjugative interaction between the two substituents can delocalise electron density from C(7), thus reducing the resonance contribution to the effective electron density.

In cross conjugated systems e.g. ylide (88) the effect of delocalisation does not reduce the %R value as much as in the acetophenones, whereas the styrene system is different from the carbonyl and nitro compounds in that it can undergo conjugative interactions with all types of substituent but paradoxically it does not experience exceptionally strong interactions with any type of substituent e.g. unlike that between NH_2 and $COCH_3$ in p-amminoacetophenone; hence delocalisation only reduces the %R from 50% to 14% in styrenes whereas in acetophenones it becomes negative.

As a final point it should be noted that the S.C.S./ charge density scaling factors for the ylides (78) - (88) and the para-substituted acetophenones 355 and 288 p.p.m./e respectively were higher than the corresponding styrene value, 200 p.p.m./e. From equation (1) these scaling factors are consistent with lower Δ E values for the carbonyl systems with respect to styrene, as the value of Δ E will determine the magnitude scaling factors. This suggests that the low energy

$n \rightarrow \pi^*$ transitions in the carbonyl systems will contribute to ΔE.

It has been shown that changes in ΔE can potentially make the largest contribution to the overall shielding. Sardella and Stothers[135] have reported the $n \rightarrow \pi^*$ transition energies for a representative selection of para-substituted acetophenones. These values suggest that π donating substituents can, via ΔE changes, cause upfield shifts while π electron withdrawing substituents cause downfield shifts. The trend is in the correct direction to explain deviations from a plot of C(7) S.C.S. values and π nuclear electron densities although in aromatic systems the transition energies of $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ being similar, $n \rightarrow \pi^*$ transitions cannot be assumed unequivocally to dominate the value of ΔE, as is found in aliphatic systems.[131,132] Further, the range of $n \rightarrow \pi^*$ transitions between para methoxyacetophenone and para nitroacetophenone (28 n.m.) is probably too large to account for a chemical shift change of ca. 2 p.p.m.; the value 1 p.p.m./n m accounted for the chemical shift variation in bicyclic ketones.[132]

S.C.S. values for carbon atoms α to a benzene ring in meta substituted systems.

Very little work has been undertaken to establish the factors affecting the chemical shifts in meta disubstituted systems. The assumption that the inductive effect via the π framework controls the magnitude of these shifts is unrealistic owing to the large range of chemical shifts observed and accordingly correlation is found with both F and R for the S.C.S. values of C(7) of the following series of meta-substituted compounds; ylides (88) - (96) acetophenones (125) - (133), Table (45). In each case the D.S.P. correlation indicated that the %R value was very close to that found for Hammett constant, σ_M (22%).[48]

As for the para-substituted series we note that the C(7) S.C.S. in meta substituted ylides (88) - (96) and acetophenones correlate in the 'wrong' sense with the respective σ electron densities on C(7) i.e. an increase in electron density causes a downfield shift. However, inspection of the values in Table (38) indicates that changes in σ electron density are slightly greater than changes

in π electron density (ca. 1.2:1).

The π electron densities of C(7) meta-substituted acetophenone derivatives are almost exclusively transmitted by the field effect of the substituent (6.6%R). Changes in π electron density at C(7) in this system cannot, by themselves, account for the observed chemical shift ranges as this would imply that a chemical shift/charge density scaling factor of 440 p.p.m./e is operative; the value 288 p.p.m./e was found for para-substituted acetophenones. However, it is probable that the changes in π electron density contribute significantly to the overall shielding of C(7).

The most likely mechanism which accounts for a field effects transmitted via the π system is the π-polarisation mechanism suggested by Reynolds.[114,115] We accept Reynold's arguments for proposing this mechanism in para-substituted styrenes and we believe that it accounts for the field contribution to the S.C.S. values of the meta and para-substituted aromatic systems discussed in this work.

Using the scaling factor derived for the para-substituted acetophenones (288 p.p.m./e) it is calculated that an electron density range of 92×10^{-4}e brings about the observed range of chemical shifts at C(7) in meta-substituted acetophenones. The equation:-

$$\Delta = 1.0\, q_Z + 1.0\, p_Z$$

reproduces the C(7) chemical shift trend fairly well ($r = 0.976$) and accounts for the resonance contribution to the observed S.C.S. However, the electron density range is too small to account for the observed S.C.S. range and hence there must be other contributions to the effective electron density of C(7) in meta-substituted acetophenones.

There have been two previous studies[123,128] of the factors affecting the ^{15}N chemical shifts of meta-substituted anilines; one group[123] suggested that changes in the π electron densities on nitrogen calculated by the Huckel method[209] for a wide range of substituents could account for these changes; the second approach[128] demonstrated that methyl substitution brought about changes in the ^{15}N chemical shifts of toluidines and xylidenes which were best rationalised by changes in the total, ($\sigma + \pi$), electron density on nitrogen.

We have performed C.N.D.O./2 calculations (Table 46) on the series of meta-substituted anilines for which ^{15}N chemical shifts are available and have found that the best correlation between chemical shift and electron density is obtained by considering changes in the total electron density ($r = 0.980$). We also note that σ electron density makes a larger contribution to the total electron density than the π electron density and changes in the σ and π electron densities occur in the correct direction to bring about the observed chemical shifts.

These results indicate a significant difference in the mode of electronic transmission from a substituent, to C(7) in a meta-substituted carbonyl system, and to the amino group in meta-substituted anilines.' The differences in mechanism could arise from two possible sources. The amino group is a terminal group and electron donating whereas the carbonyl group is electron withdrawing and C(7) is not the terminal atom in the system.

S.C.S. values of carbons β to a benzene ring in para substituted systems.

There have been several reports of successful correlations of π nuclear charge density and the β-carbon chemical shifts in para-disubstituted aromatic systems. This is exemplified by examination of the styrene system (11)[114] where the S.C.S./electron density scaling factors for C(8) were adequate for both field and resonance contributions. This implies that changes in bond order have little influence on the effective electron density which contributes to the C(8) chemical shift in para-substituted styrenes. This may be rationalised by examination of the magnitudes of the C(7), C(8) π electron densities and the C(1) - C(7), C(7) - C(8) π bond orders in Table (39). It is apparent that the relative effect of changes in the C(1) - C(7) π bond order will have a greater effect on the effective electron density at C(7) than the effect of comparable changes in the C(7) - C(8) π bond order on the effective charge density at C(8).

In para-disubstituted aromatic systems in which one of the substituents extends the conjugation of the ring it is found that the S.C.S. values of the β atom in this substituent show a reasonable linear relationship with Hammett constant σ_p

which implies that the %R in the S.C.S. values is ca. 50%. Phillips[49] has proposed that σ_p was a measure of the transmission of electronic effects via the π system to a distant atom.

Examination of the S.C.S. values for the methyl carbons in para-substituted acetophenones and C(8) in the arsonium ylides indicates that there is about the same %R weighting in the D.S.P. correlation for both series, ca. 70%, whereas that for C(8) in the phosphonium ylides is 55.8%, Tables (41),(42).

The trend in the chemical shift is in the same sense as for the chemical shifts of C(1) i.e. π electron withdrawing substituents cause downfield shifts.

The %R value for the S.C.S. of the acetyl methyl carbons in para-substituted acetophenones (76.2%R) is of the same order of magnitude as that previously found for the ^{1}H S.C.S. of the attached protons (70.9%), suggesting that there are no significant magnetic contributions to the chemical shifts of the acetyl methyl protons. Further, the mechanism of electronic transmission to C(8) and its attached protons is either the same, or electron density changes on C(8) control the chemical shifts of the attached protons.

The high %R value for C(8) in these systems is inconsistent with electronic effects transmitted through the π system, where a figure of ca. 50%R is indicative of this type of transmission. Changes in the p_z electron density on C(8) of para-substituted acetophenones occur in the 'wrong' direction to rationalise the changes in chemical shift observed for this carbon atom.

In aromatic systems a change in C(4) substituent induces a large change of electron density on the para carbon atom C(1). These changes have been postulated as being the source of the ^{1}H S.C.S. of H(7) in styrenes (11) by means of variation in electron density brought about by through space effects. Since changes in electron density at C(1) are dominated by resonance effects (74%R) then a high %R value is expected for the S.C.S. of H(7); this result was found by Reynolds.[114]

The C(8) methyl carbons of para-substituted acetophenones

are formally joined by a single bond to the π system. Since calculations indicate that electronic transmission probably does not occur via the π system, Table (40), it is possible that the S.C.S. values for C(8) in para-substituted acetophenones occur by similar mechanism to those of H(7) in styrenes. If this is true, then substituent effects at C(8) should comply with Batchelor's[178] theory of electric field chemical shifts for ^{13}C shifts.

The relevant points of this theory which are applicable to this case are that changes in the electric field at C(1) with a component in the W direction, figure 9, will cause changes in the electron density at C(8)

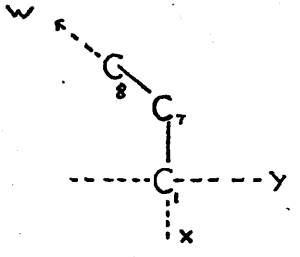


fig. (9)

electron density

Changes in the p_Z of C(1) will not affect the C(8) chemical shifts as it has no component in the W direction, as W and Z are perpendicular. Hence changes in the x, y plane of C(1) will be expected to induce the changes at C(8).

The σ (x, y) electron density is believed to arise by π - σ polarisation,[206] hence a π electron withdrawing substituent at C(4) induces an increase in the x, y electron density at C(1).

An upfield uniform linear electric field shift[178] is caused by a positive charge on the negative side of the plane perpendicular to the W direction in figure (7). The positive side of this plane is the side containing the most polarisable bonds i.e. the C - H bonds. Hence π electron donating substituents should cause upfield shifts relative to acetophenone and π donating substituents should cause downfield shifts, as observed.

The changes in σ electron density at C(8) are in the correct sense to explain these changes, the S.C.S./electron density scaling factor is acceptable (285 p.p.m./e), however the observed trend is not exactly reproduced.

From the %R values of the C(8) S.C.S. of phosphonium ylides (134) - (141) and arsonium ylides (142) - (150) it

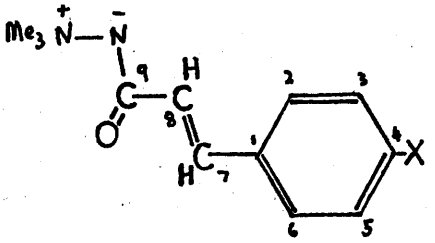
would seem probable that the C(7) - C(8) bond in the phosphonium ylide has more double bond character than that in the arsonium ylide as the former compounds have a %R value close to that associated with Hammett constant σ_p indicating dominant transmission via the π system. Molecular orbital calculations do not support this proposition.

Finally it should be noted that C(8) S.C.S. ranges in (134) - (141) and (142) - (150) are more than three times as large as those of C(8) in para-substituted acetophenones, Tables (35) and (37).

S.C.S. values for the acetyl methyl carbons in meta substituted acetophenones.

The range of ^{13}C chemical shifts of the methyl carbons of meta substituted acetophenones is extremely small (0.2 p.p.m.). This carbon atom is one atom nearer the substituent than C(8) in para substituted acetophenones, yet in the para case the range of S.C.S. of C(8) is about five times the range of the S.C.S. of C(8) in the meta system.

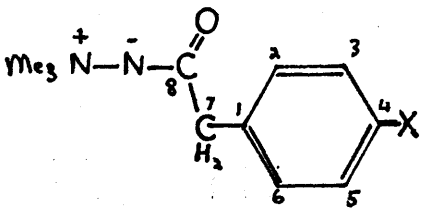
This observation suggests that the methyl carbons in meta substituted acetophenones are dominated by two or more modes of electronic transmission acting in opposition, reducing the effective chemical shift range. This type of effect was demonstrated for the C(7) chemical shifts in para substituted acetophenones, where changes in the π bond orders reduces the effective charge density and decreases the observed S.C.S. range.



X = H : 151 X = Cl : 154 X = NO_2 : 157

X = Me : 152 X = F : 155 X = NMe_2 : 158

X = ome : 153 X = CN : 156



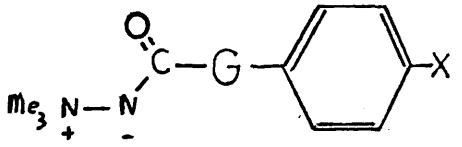
X = H : 159 X = Cl : 162 X = NO_2 : 165

X = me : 160 X = F : 163

X = ome : 161 X = Br : 164

^{13}C CHEMICAL SHIFTS OF PARA-SUBSTITUTED 1′, 1′, 1′ TRIMETHYLAMMONIO 2′-CINNAMOYLIMIDES AND 2′-PHENYLACETIMIDES.

We have used the ^{13}C chemical shifts of para-substituted cinnamoyl ylides (151) - (158) and phenylacetyl ylides (159) - (165) as probes for the transmission of electronic effects through a molecular cavity (G)



G = -CH=CH- ; X = H : (151)

G = $-CH_2-$; X = H : (159)

Previously ^{19}F chemical shifts were used for this type of work[211,49] e.g. to study electronic effects in systems such as (2).[211] However, an investigation by Taft's group[53] has indicated that, since the fluorine atom in (2) is accessible to the solvent, this molecule is readily solvated and the electron withdrawing capabilities of the fluorine are enhanced through increased field effects leading to anomalous substituent effects.

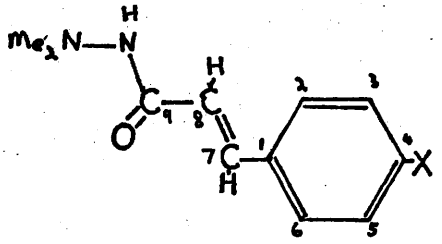
In our system the probe atom, the carbonyl carbon atom C(9), is shielded from the solvent and at low sample concentrations the S.C.S. values should be free from solvent effects.

The O = C - N - $N(Me_3)$ group has already been shown to exert similar electronic effects on a juxtaposed aromatic ring as a nitro group, and therefore, as compounds containing the former group are readily available, they provide a convenient means of assessing the effect of a group which is electron withdrawing by field and resonance effects on electronic transmission through an extended conjugated system (151) and one in which conjugation between the substituent and the probe group is minimised (159).

1) Para-substituted cinnamoyl ylides.

The ^{13}C chemical shifts of the para substituted cinnamoyl ylides (151) - (158) are given in Table (47) and the results of C.N.D.O/2 molecular orbital calculations on these compounds using structure (183) are given in Table (48).

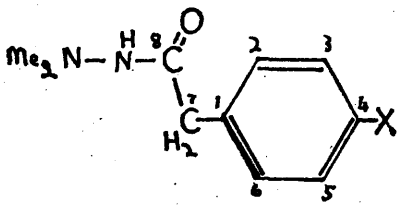
The ^{13}C n.m.r. spectra of these compounds were assigned in an analogous manner to that used for the benzoyl ylides



X = H : 166 X = Cl : 169 X = NO_2 : 172

X = Me : 167 X = F : 170 X = NMe_2 : 173

X = OMe : 168 X = CN : 171



X = H : 174 X = Cl : 177 X = No_2 : 180

X = Me : 175 X = F : 178

X = OMe : 176 X = Br : 179

(78) - (88). In addition specific proton decoupling of the β-vinyl proton allowed identification of the β -carbon atom, and thus also the α-carbon could be assigned.

We also recorded the ^{13}C n.m.r. spectra of the series of para substituted 1′, 1′, dimethyl 2′-cinnamoyhydrazides (166) - (173), however the signals for C(7), C(8), C(9) were split by restricted rotation and so these compounds were not suitable for this type of investigation.

As expected, the S.C.S. values for C(7), C(8) in compounds (151) - (158) show a similar trend to the S.C.S. of the respective carbons in para-substituted styrenes (11).[114] D.S.P. correlations with F and R, Table (51) show that the %R values for C(8) in the cinnamoyl ylides and styrenes are identical (61%), however the chemical shift range in (151) - (158) is slightly greater by a factor of 1.1:1. Examination of the π electron densities for the two series indicates that the increase in S.C.S. values for the cinnamoyl ylides is paralleled by a similar increase in the π electron density range, Tables (39), (48).

The C(7) S.C.S. range in the cinnamoyl ylides (2.77 p.p.m.) is greater than that of C(7) in styrenes (1.93 p.p.m.). For this carbon atom in the two series the %R of the S.C.S. in each is different. The value 35.6%R for the cinnamoyl ylides as opposed to 14%R in the styrenes indicates that delocalisation changes <u>via</u> changes in bond order are not so important in former system as they are in styrenes. This results from an increased electron density range on C(7) in (151) - (158) relative to that for C(7) in styrenes while the C(7) - C(1) π bond order for the two series remains constant, Tables (39) - (48).

Hence for the C(7) S.C.S. of (151) - (158) the equation:-

$$\Delta = 0.5\, q_Z + p_Z$$

approximately reproduces the observed trend with a chemical shift/electron density scaling factor of 213 p.p.m./e.

The S.C.S. values of the carbonyl carbon C(9) in compounds (151) - (159) have a %R value of 58.2%. This implies that transmission of electronic effects occurs <u>via</u> the π system and changes in the π electron density produce this trend fairly well and gives a scaling factor of 264 p.p.m./e.

The results for these three carbon atoms suggest that the

cinnamoyl ylide is planar and electronic transmission occurs via the π system.

Para-substituted phenylacetyl ylides.

The ^{13}C chemical shifts of the phenylacetyl ylides (159) - (164) are given in Table (49). The assignment of the ^{13}C n.m.r. spectra of these compounds was straightforward and the ^{13}C chemical shifts of the ring carbons are assigned as for the other ylide systems we have studied e.g. (78) - (88). The results of relevant C.N.D.O/2 calculations on these ylides using structure (184) are given in Table (50).

The S.C.S. values for C(7) in the phenylacetyl ylides contain a very high resonance contribution (89%R). The most likely mechanism for this is σ polarisation arising from changes at C(1), although we note that the C(1) S.C.S. only contains ca. 75%R . Changes in the total electron density at C(7) best account for the observed trend, the electron density/chemical shift scaling factor is 265 p.p.m./e. Data for the methyl S.C.S. of 4-substituted toluenes[212] suggests that similar effects control the S.C.S. of this carbon atom as those which bring about the S.C.S. of C(7) in (159) - (164).

The S.C.S. values of C(8) in (159) - (164) contain a resonance contribution (51.5%R) which is close to that expected for transmission via a π system (53%R).[50] This result is unexpected as conjugation between the carbonyl and the benzene ring is formally blocked by the methylene group C(7). We also note that the S.C.S. range at C(8) is greater than that at C(7).

Following from a study of the conformations of a series of substituted benzene derivatives,[168] we have assumed that the C(1) - C(7) - C(8) plane in (184) is at 90° to the mean plane through the benzene ring and have performed C.N.D.O/2 calculations using this geometry.

Electron density changes in the Z direction on C(7) are in the 'wrong' sense to bring about the observed S.C.S. values while changes in the X, Y plane are too small to account for the observed trend, Table (50).

The ^{19}F S.C.S. values of para-substituted benzyl fluorides[212] show a similar trend to the S.C.S. values of C(8) in (159) - (165) and it appears that in a system of this

type the presence of a $-CH_2-$ does not prevent electronic transmission via the π system from occurring. Taft[211] has attributed this to the presence of pseudounsaturation present in 'formally saturated' cavities.

Although the mechanism of transfer of substituent effects appears to occur via the π framework the efficiency of this process is many times less efficient than in a system involving extended conjugation e.g. compare S.C.S. ranges of C(8) in (159) - (164), Table (50) and styrenes.[114]

SUBSTITUENT EFFECTS ON THE LONG RANGE PROTON-PROTON COUPLING CONSTANTS IN 4-SUBSTITUTED CAMPHORS.

Spin-spin coupling between two protons A and B occurs through the interaction of the spins on A interacting with those on B and these interactions affect the field experienced by protons A and B. Both these protons can occupy one of two spin states; parallel or antiparallel. Thus there are four possible combinations of spin states for A and B each affecting the field experienced by protons A and B to a different extent. These interactions are the source of the spin multiplets observed in an n.m.r. spectrum.

The magnitude of the difference in field that the various spin-interactions bring about on the resonance position of a given proton is called the spin-spin coupling constant, J, and unlike the chemical shift, its value is unaffected by frequency of irradiation.

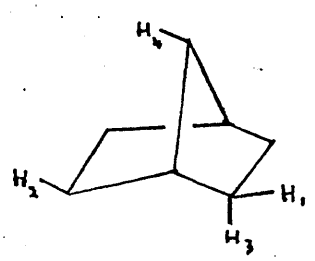
Coupling constants have been observed between protons separated by up to nine bonds.[214] The value of the coupling constant generally decreases for larger proton separations.

Spin-spin couplings for protons separated by two, three and four bonds are termed geminal, vicinal and long range couplings respectively.

For geminal and vicinal proton couplings in organic compounds it has been shown that the factors[215] affecting the magnitude of J are, the relative orientation of the two protons with one another and any substituents, the hybridisation of carbon atoms in intervening bonds, and the substituent electronegativity.

Two reviews of this subject have appeared,[215,217] one[216] collates the better established correlations, relating the magnitudes of $^4J_{H-H}$ to structure in an empirical manner, while the other[214] attempts to derive values of $^4J_{H-H}$ on a quantum mechanical basis.

There is a favourable geometrical disposition of protons[216] which gives rise to large long range



(185)

coupling interactions, the so called W or M configuration i.e. between H(1) and H(2) or H(3) and H(4) in (185) which has the four bonds in the one plane, the meta coupling in aromatic systems being a special case of this.

Three main mechanisms have been suggested to account for long range couplings.[214] A direct through space interaction between the coupled nuclei, a 'through the bonds' mechanism and an additional rear lobe type interaction, figure 10, when

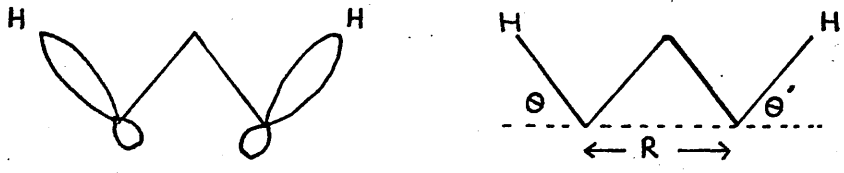


Fig. 10

the two protons are in the W configuration.

Sardella[217] has shown that the magnitude of vicinal and long range coupling constants in substituted propanes both exhibit linear relationships with substituent electronegativity as indicated by the electronegativity parameter, E_R. The magnitudes of coupling constants decrease and increase respectively with increasing substituent electronegativity and the variation in long range coupling constants are attributed to changes in singlet - triplet excitation energies.

The effect of the conformation of coupled protons on the magnitudes of the long range coupling constants has been investigated[218] and it is calculated that positive $^4J_{H-H}$ values are found only for a small range of values near the all trans (W) orientation of coupled protons. The results of these calculations also demonstrate that, if the C(1) - C(2) - C(3) angle in a propanic system is increased to 120°, the coupling constants for conformations corresponding to the all-trans arrangement decreases by a factor ca.3, but those corresponding to other conformations remain fairly constant. This was taken to imply that large positive values which occur in the all-trans orientation can be attributed to a direct interaction between bonds associated with the coupled nuclei, rather than the 'rear lobe' interactions of carbon hybrids and the direct mechanism becomes less important when

the four atom fragment is not coplanar.

A study of the conformational dependence of $^4J_{H-H}$ in cyclic systems[219] indicates that the magnitude of the long range coupling constant and the square of the bond order (calculated using the I.N.D.O. approximation) between the protons both increase in value as a cyclobutane ring buckles.

An empirical calculation[219] to assess the magnitude of electron overlap for the coplanar situation, indicating the importance of the direct mechanism, shows that the value of $^4J_{H-H}$ is directly proportional to $\frac{\cos\theta \cos\theta'}{R}$, figure (10).

Finally, the effect of the position of substitution has been investigated. Barfield[218] has calculated that in substituted propanes inductive or hyperconjugative substituents at C(2) generally produces a positive shift of the long range coupling constant; however a hyperconjugative substituent, e.g. CN, at C(1) causes a negative shift, whereas an inductive substituent at this position causes a positive shift. This is in agreement with the simple qualitative model that removal of electrons via σ acceptor or back donation by a suitably orientated π type orbital will cause an algebraic increase in the value of $^4J_{H-H}$ whereas electron withdrawal via a π orbital will cause $^4J_{H-H}$ to decrease.

Sardella[220] has shown that the values of $^4J_{H-H}$ for a series of 2-substituted t-butyl groups were inversely proportional to those of a 1-substituted neo-pentyl system and also that for the mono-substituted propanes any type of substituent should cause an increase or decrease in value of $^4J_{H-H}$ when substituted on C(2), C(1) respectively and this cannot be explained by charge alternation.[221] Therefore, electron redistribution at the orbital level must be considered in rationalising these changes.

In the present work we have examined the 100 MH_z ^1H n.m.r. spectra of a series of 4-substituted camphors (45) - (55) Table (52). In this series the C(1) and C(7) methyl groups perform the useful role of removing certain long range proton-proton couplings. The value of $^4J_{H-H}$ in strained bicyclic systems is typically larger than in their

acyclic or monocyclic counterparts. Thus values of *ca.* 1.5 Hz are found for $^4J_{H3\ exo - H5\ exo}$ in camphors while the presence of electronegative substituents enhance $^4J_{H3\ exo - H5\ exo}$ to 3.0 Hz in 2, 7 dioxabicyclo [2.2.1.] heptanes.[222]

First order analysis of the spectra of camphors (45) - (55) indicated that spin coupling of $H_{3\ exo}$ to $H_{3\ endo}$ gave rise to an A B pattern, the low field A component of which was further split by long range coupling of $H_{3\ exo}$ with $H_{5\ exo}$. The assignment of $H_{3\ exo}$ to the low field component was substantiated by specific deuteration in the *exo* position of C(3) in (45), (51) and (53).

The chemical shifts of $H_{3\ exo}$ and $H_{3\ endo}$ appear in a clear region of the spectrum at positions downfield from the remaining methylene protons. Further evidence that the additional splitting of $H_{3\ exo}$ was caused by spin coupling interactions was obtained by decoupling experiments.

Values of $^4J_{H3\ exo - H5\ exo}$ for the camphors (45) - (55) are given in Table (52) and line positions within the partially split A B pattern are given in Table (2).

Inspection of the values of ^4J indicates that its value increases with an increasing of the substituent electron withdrawing power. Whereas other groups have found linear relationship between the value of ^4J and the group electronegativity, E_R, of the substituent[216,217] we find that such a correlation is only moderate for the coupling constants observed here. Alternatively, we have correlated $^4J_{H3\ exo - H5\ exo}$ with the inductive linear free energy parameter, σ_I, ($r = 0.978$). The correlation embraces a wide range of substituent character and a wider range of ^4J is encompassed than previously. Although the bicyclo [2.2.1.] heptane skeleton is frequently thought of as completely rigid, deviations of up to 10° have been reported.[182] However, it is likely that a change of substituent at C(4) will cause negligible changes in ring structure and variations in $^4J_{H-H}$ may be completely ascribed to substituent effects.

With the proviso that the signs $^4J_{H3\ exo - H5\ exo}$ are always positive, the substituent effects are in agreement with those found previously,[216,217] and calculations have

suggested for the all-trans, W, conformation that the value of $^4J_{H-H}$ is always positive.[218]

A planar, W, disposition of atoms has been considered as optimum for the manifestation of long range coupling, although it has been noted in many instances that large values of $^4J_{H-H}$ are observed where deviations from this conformation occur.[214] In endo-3-bromocamphor[165], for which structural data are available, the angle between the planes H_3 exo - C(3) - C(4) and C(4) - C(5) - H_5 exo is 8.4° and, although skeletal geometry may vary slightly, it is expected that the corresponding camphors (45) to (55) would be similar.

We note only minor variation in the geminal coupling constant $^2J_{H3\ exo - H3\ endo}$ for camphors (45) - (55), Table (52).

In order to assess the role of the carbonyl group in determining the magnitude of $^4J_{H3\ exo - H5\ exo}$ we have prepared the nitrimines (67), (68), (69) and (71)(Table (53). Nitrimines are capable of configurational isomerism and, although formal proof is lacking, it is probable, from consideration of models, that these compounds exist in the configuration which places the C(2) - C(3) bond syn to N-N bond. However, the near constancy of the downfield shifts for both the C(3_{exo}) and C(3_{endo}) protons in the nitrimines with respect to the corresponding camphors, Tables (52) and (53) supports a common configuration for (67), (68), (69) and (71). It was not possible to gain information bearing on the configuration of (67), (68), (69) and (71) by an analogous comparison of the shifts of the C(10) methyl protons on account of the difficulty of assigning the C(8), C(9) and C(10) methyl proton absorptions. However, in the ^{13}C n.m.r. spectra of (67), (68), (69) and (71) C(10) absorbs 1.1 to 1.2 p.p.m. downfield from C(10) in the corresponding ketone and we have interpreted this result as implying that a common configuration obtains in which C(2) and C(3) and the N-N bonds are syn.

TABLE 1.

SUBSTITUENT PARAMETERS

Substituent	E_R[a]	σ_I[b]	σ_M[c]	σ_P[c]	F[d]	R[d]	σ^o_R[b]
H	2.1	0	0	0	0	0	0
Me	2.3[e]	-0.04	-0.07	-0.17	-0.052	0.155	-0.11
F	3.93[e]	0.50	0.34	0.06	0.708	-0.336	-0.34
Cl	3.25	0.46	0.37	0.23	0.690	-0.161	-0.23
Br	2.96	0.44	0.39	0.23	0.727	-0.176	-0.19
OH	3.5[F]	-	0.00	-0.36	0.487	-0.643	-0.16
OMe	-	0.27	0.12	-0.27	0.413	-0.500	-0.45
NH_2	2.91	0.12	-0.16	-0.66	0.037	-0.681	-0.48
NMe_2	-	0.06	-0.21	-0.60	-0.097[g]	-0.568[g]	-0.52
COOH	2.6	0.30	0.36	0.26	0.552	0.140	0.14
COME	-	0.28	0.31	0.52	0.534	0.202	0.16
CH_2OH	-	0.09[h]	-	-	-	-	-
NO_2	3.70[f]	0.65	0.71	0.78	1.109	0.155	0.15
CF_3	-	0.45	0.42	0.55	0.631	0.186	0.08
CN	2.49	0.56	0.68	0.63	0.847	0.184	0.13

NOTES

(a) Ref.39

(b) Ref.47 page 13.

(c) Ref.40 page 28.

(d) Ref.48

(e) Ref.38

(f) Ref.217

(g) Ref.114

(h) M.Charton, J.Org. Chem., 1964, 29, 1222.

TABLE 2.

^1H Line positions of 4-SUBSTITUTED CAMPHORS (46) - (55) AND CAMPHORNITRIMINES (67) - (71) AT 100 M Hz IN p.p.m. DOWNFIELD FROM TETRAMETHYLSILANE.

Compound	H_3 exo				H_3 endo	
(46)	2.20	2.18	2.02	2.00	1.93	1.74
(48)	2.58	2.54	2.39	2.36	2.24	2.06
(49)	2.95	2.91	2.76	2.73	2.26	2.08
(55)	2.90	2.86	2.71	2.67	2.17	1.99
(50)	2.91	2.87	2.73	2.69	2.20	2.02
(51)	2.75	2.72	2.57	2.54	2.46	2.28
(52)	2.83	2.80	2.65	2.62	2.52	2.35
(53)	3.39	3.35	3.21	3.17	2.61	2.43
(67)	2.54	2.51	2.35	2.33	2.22	2.04
(71)	3.28	3.25	3.09	3.06	2.55	2.36
(69)	3.74	3.70	3.55	3.51	2.93	2.74
(70)	3.06	3.03	2.87	2.84	2.75	2.56

TABLE 2 Cont'd

Compound	Methyl chemical shifts			
(46)	1.04	0.92	0.84	0.71
(48)	0.96	0.92	0.82	
(49)	1.07	0.97	0.92	
(55)	1.05	0.93	0.87	
(50)		0.95	0.91	
(51)	0.99 (6H)		0.88	
(51)	1.01	0.99	0.89	
(53)	1.12	1.00	0.95	
(67)	1.06	1.00	0.86	0.76
(71)	1.10 (6H)		0.95(3H)	
(69)	1.17 (6H)		1.00(3H)	
(70)	1.12	1.01	0.91	

TABLE 3.

U.V. DATA FOR CAMPHORS

Compound	$\lambda_{max.}$ (MeOH)	ε
(45)	289	32
(48)	285.5	35
(51)	288	32
(53)	283	81

NOTE: For (53) the absorption band probably contains contributions from both the carbonyl and nitro groups.

TABLE 4.

ANALYTICAL DATA FOR PARA-SUBSTITUTED 1′, 1′-DIMETHYL 2′- BENZOYLHYDRAZIDES (97) - (106)

δ ($CDCl_3$) 6.5 - 8.0 (4H,m), 2.7 - 2.8 (6H,s),
(97) 2.4 (3H,s), (98) 3.9 (3H,s)
(105) 3.0 (6H,s)

$\nu_{max.}$ (Nujol) 1630 - 1680 cm^{-1}

Compound	m.p.	Found %			Required %		
		C	H	N	C	H	N
(106)	104-5 (lit.,[a] 105-7)						
(97)	109-10	67.26	7.94	15.76	67.39	7.92	15.72
(98)	110-11	61.87	7.55	14.65	61.84	7.27	14.42
(99)	101-2	59.00	6.26	6.08	59.32	6.08	15.38
(100)	132-3	54.43	5.65	13.90	54.43	5.58	14.11
(101)	148-50	44.54	4.46	11.47	44.46	4.56	11.53
(102)	129-30	51.97	4.75	12.05	51.8	4.75	12.05
(103)	149-50	51.41	5.44	20.47	51.67	5.30	20.09
(104)	144-5	63.50	6.03	21.94	63.47	5.86	22.21
(105)	139-41				63.74	8.27	20.27

a) R.F.Smith, A.C.Bates, A.J.Battisti, P.G.Byrnes, C.T.Mroz, T.J.Smearing and F.X.Allricht, J.Qrg. Chem., 1968, 33, 851.

TABLE 5.

ANALYTICAL DATA FOR PARA-SUBSTITUTED 1′, 1′, 1′-TRIMETHYLAMMONIO 2′-BENZIMIDES (78) - (88).

δ ($CDCl_3$) 6.5 - 8.0 (4H,m) 3.5 (9H,s)
(79) 2.4 (3H,s), (80) 3.93 (3H,s)
(78) 3.0 (6H,s)

$\upsilon_{max.}$ (Nujol) 1600 - 1640 $cm.^{-1}$

Compound	m.p. °C	Found %			Required %		
		C	H	N	C	H	N
(88)	169-70 (lit.,[b] 170)						
(79)	133-4	68.44	8.56	14.42	68.72	8.39	14.57
(80)	142-3	63.68	7.86	13.29	63.44	7.74	13.45
(81)	174-5	61.37	6.71	14.29	61.22	6.60	14.29
(82)	103-4	56.62	6.29	13.26	56.46	6.16	13.17
(83)	104-6	46.77	5.32	10.94	46.70	5.06	10.88
(84)	153-4	53.58	5.25	11.62	53.7	5.3	11.28
(85)	221-2	54.09	5.91	19.08	53.80	5.87	18.83
(86)	160-1	75.73	7.06	11.02	75.56	7.13	11.02
(87)	203-5	65.06	6.44	20.77	65.01	6.45	20.67
(78)	147-8	65.26	8.77	18.62	65.12	8.65	18.99

b) M.S.Gibson and A.W.Murray, J.Chem.Soc., 1965, 880.

TABLE 6.

ANALYTICAL DATA FOR META-SUBSTITUTED 1′, 1′-DIMETHYL 2′-BENZOYLHYDRAZIDES (107) - (115).

δ ($CDCl_3$) 6.6 - 8.2 (4H,s), 2.7 (6H,s),
(107) 2.4 (3H,s), (108) 3.8 (3H,s),
(115) 3.0 (6H,s).

$\upsilon_{max.}$ (Nujol) 1630 - 1650 $cm.^{-1}$

Compound	m.p. °C	Found %			Required %		
		C	H	N	C	H	N
(107)	90-1	67.66	7.99	15.96	67.39	7.92	15.72
(108)	95-6	61.90	7.37	14.15	61.84	7.27	14.42
(109)	92-3	59.53	6.36	15.25	59.32	6.08	15.38
(110)	100-2	54.60	5.63	13.85	54.43	5.58	14.11
(111)	100-1	44.60	4.62	11.69	44.46	4.56	11.53
(112)	95-6	51.99	5.17	11.32	51.80	4.75	12.05
(113)	157-8	51.44	5.09	20.15	51.67	5.30	20.09
(114)	110-12	63.36	5.99	22.40	63.48	5.86	22.21
(115)	97-98	63.36	8.46	19.80	63.74	8.27	20.27

TABLE 7.

ANALYTICAL DATA FOR META-SUBSTITUTED 1′, 1′, 1′ - TRIMETHYLAMMONIO 2′-BENZIMIDES (89) - (96)

δ ($CDCl_3$) 6.7 - 8.33 (4H,m), 3.5 (9H,s)
(97) 2.4 (3H,s), (98) 3.8 (3H,s).

$\upsilon_{max.}$ (Nujol) 1600 - 1620 $cm.^{-1}$

Compound	m.p. °C	Found %			Required %		
		C	H	N	C	H	N
(89)	103-4	68.81	8.36	14.50	68.72	8.39	14.57
(90)	112-3	63.18	7.77	13.57	63.44	7.74	13.45
(91)	93-4	61.44	6.90	14.71	61.22	6.60	14.29
(92)	114-6	56.67	6.45	13.18	56.46	6.16	13.18
(93)	100-1	45.9	4.72	11.82	45.97	4.72	11.92
(94)	143-5	54.48	5.58	11.48	53.71	5.30	11.28
(95)	152-3	52.98	5.98	18.00	53.81	5.87	18.82
(96)	108-10	64.90	6.62	21.11	65.01	6.45	20.67

TABLE 8.

ANALYTICAL DATA FOR PARA-SUBSTITUTED 1′, 1′-DIMETHYL 2′-PHENYLACYLHYDRAZIDES (174) - (180).

δ ($CDCl_3$) 6.6 - 7.5 (4H,m) ; 2.4 - 2.6 (6H,split by restricted rotation) ;
3.4 - 3.9 (2H, split by restricted rotation)
(175) 2.3 (3H,s) ; (176) 3.82 (3H,s)

$\nu_{max.}$ (Nujol) 1650 - 1670 cm^{-1}.

Compound	m.p.°C	Found %			Required %		
		C	H	N	C	H	N
174	102-3	67.65	7.93	15.9	67.38	7.92	15.72
175	104-5	68.88	8.43	14.38	68.72	8.39	14.57
178	138-9	61.0	6.80	14.48	61.23	6.68	14.29
179	146-7	47.00	5.33	10.96	46.70	5.09	10.90
180	165-8	53.69	6.05	18.62	53.80	5.87	18.33
177	145-6	56.77	6.24	13.22	56.48	6.16	13.17
176	127-8	63.46	7.68	13.51	63.44	7.74	13.45

TABLE 9.

ANALYTICAL DATA FOR PARA-SUBSTITUTED 1′, 1′, 1′-TRIMETHYLAMMONIO 2′- PHENYLACYLIMIDES (159) - (165).

δ ($CDCl_3$) 6.6 - 8.2 (4H,s) ; 3.3 - 3.5 (11H,2s)
(160) 2.40 (3H,s) ; (161) 3.8 (3H,s)

$\nu_{max.}$ (Nujol) 1590 - 1600 cm^{-1}.

Compound	m.p.°C	Found %			Required %		
		C	H	N	C	H	N
160	75-6	69.9	8.80	13.73	69.85	8.79	13.58
162	103-4	58.42	6.75	12.74	58.27	6.67	12.36
161	129-30	64.80	8.16	12.90	64.82	8.16	12.60
165	154-5	55.21	6.35	17.50	55.49	6.37	17.71
159		Hygroscopic			68.72	8.39	14.57
163		Hygroscopic			62.84	7.19	13.33
164	47-8				48.70	5.58	10.33

TABLE 10.

ANALYTICAL DATA FOR PARA-SUBSTITUTED 1′, 1′-DIMETHYL 2′-CINNAMOYLHYDRAZIDES. (166) - (173)

δ ($CDCl_3$) 6.5 - 8.3 (6H,m) ; 2.4 - 2.6 (6H,split by restricted rotation),
(167) 2.3 (3H,s) ; (168) 3.8 (3H,s) ; (173) 2.8 (6H,s)

$\upsilon_{max.}$ (Nujol) 1580 - 1610 cms^{-1}.

Compound	m.p. °C	Found %			Required %		
		C	H	N	C	H	N
166	110-11	69.28	7.34	14.97	69.44	7.42	14.73
167	144-5	70.53	8.04	13.73	70.56	7.90	13.71
170	125-8	63.08	6.45	13.22	63.36	6.29	13.45
173	183-4	66.66	8.03	17.95	66.91	8.21	18.01
168	122-3	65.45	7.41	7.32	65.43	7.32	12.72
172	171-2	55.88	5.50	17.73	56.16	5.57	17.86
169	158-9	58.69	6.00	12.68	58.79	5.83	12.46
171	183-4	66.89	6.16	19.27	66.96	6.09	19.52

TABLE 11.

ANALYTICAL DATA FOR PARA SUBSTITUTED 1′, 1′, 1′-TRIMETHYLAMMONIO 2′-CINNAMOYLIMIDES (151) - (158)

δ ($CDCl_3$) 6.6 - 8.3 (5H,m) ; 6.3 - 6.8 (1H, B part of AB quartet ; the A part is obscured by the aromatic absorptions, J_{AB} 15.0 Hz).
(152) 2.3 (3H,s) ; (153) 3.8 (3H,s) ; (158) 2.8 (6H,s)

$_{max.}$ (Nujol) 1580 - 1600

Compound	m.p. °C	Found %			Required %		
		C	H	N	C	H	N
151	224-5				70.5	7.90	13.71
152	187-8	71.27	8.10	12.77	71.50	8.30	12.83
153	168-70	64.72	8.23	12.41	64.84	8.16	12.60
155	140-1				64.84	6.80	12.60
154	168-9	60.52	6.37	11.84	60.37	6.19	11.74
157	232-3	57.51	6.3	16.77	57.81	6.04	16.86
156	217-8	68.18	6.67	18.60	68.10	6.60	18.33
158	193-4	67.96	8.34	17.21	67.98	8.55	16.99

TABLE 12.

ANALYSIS DATA FOR META AND PARA-ACETOPHENONES (116) - (133)

(118), (119), (122), (125) were commercial samples.

δ ($CDCl_3$) 6.5 - 8.0 (4H,m) ; 2.5 - 2.7 (3H,s) ;
(116),(126) 2.3 (3H,s) ; (117),(127) 3.8 (3H,s);
(124),(133) 2.8 (6H,s).

$\upsilon_{max.}$ (Nujol or liquid film) 1700 - 1720 cm^{-1}.

Compound	m.p. °C	lit.[143]	% ethyl acetate used in t.l.c
116	oil	28	10%
117	35-36	38-9	
121	oil	-	15%
123	119-20	120-1	
124	103-5	105-6	
126	oil	-	10%
127	93-95	95-6	
128	oil	-	10%
129	oil	-	10%
131	oil	-	15%
130	oil	7-8	10%
132	78-80	81-2	
133	oil	42-3	50%

TABLE 13.

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 4-SUBSTITUTED TRICYCLENES

Substituent	C(1)	C(2) C(6)	C(3) C(5)	C(4)	C(7)	C(8) C(9)	C(10)
H	26.3	20.6	31.3	41.8	43.1	19.4	9.4
Me	28.8	20.3	38.2	43.3	44.2	17.7	11.5
CH_2OH	29.1	19.9	33.8	49.0	44.2	18.5	10.7
OH	29.8	19.2	36.1	79.9	43.1	17.3	12.2
COOH	28.0	19.6	35.1	52.8	46.9	18.7	10.7
CO_2Me	27.8	19.5	34.9	52.8	46.7	18.7	10.7
COMe	28.1	19.6	35.1	60.4	46.9	18.8	10.5
Cl	27.5	19.3	39.3	69.5	45.8	17.6	12.1
NO_2	28.0	18.8	35.2	89.7	47.7	17.8	11.2
NH_2	28.7	19.9	37.9	60.6	43.8	17.2	12.3

Chemical shifts of substituents

(Me) 12.2 ; (CH_2OH) 67.7

(CO_2Me) 173.8, 51.0 ; (COMe) 210.3, 29.7

TABLE 14

^{13}C CHEMICAL SHIFT INCREMENTS (p.p.m.) OF 4-SUBSTITUTED TRICYCLENES

Substituent	C(1)	C(2) C(6)	C(3) C(5)	C(4)	C(7)	C(8) C(9)	C(10)
H	0	0	0	0	0	0	0
Me	2.5	-0.3	6.9	1.5	1.1	-1.7	2.1
CH_2OH	2.8	-0.7	2.5	7.2	1.1	-0.9	1.3
OH	3.5	-1.4	4.8	38.1	0.1	-2.1	2.8
CO_2H	1.7	-1.0	3.8	11.0	3.8	-0.7	1.3
CO_2Me	1.5	-1.1	3.6	11.0	3.6	-0.7	1.3
COMe	1.8	-1.0	3.8	18.6	3.8	-0.6	1.1
Cl	1.2	-1.3	8.0	27.7	2.7	-1.8	2.7
NO_2	1.7	-1.8	3.9	47.9	4.6	-1.5	1.8
NH_2	2.4	-0.7	6.6	18.8	0.7	-2.2	2.9

Positive values in this and other tables of shift increments indicate shift to low field.

TABLE 15

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 1-SUBSTITUTED BICYCLO [2.2.2.] OCTANES.

Substituent	C(1)	C(2)	C(3)	C(4)	C(9)
OH	69.09	33.91	27.20	24.41	
CH_2OH	32.44	27.78	25.77	24.68	71.92
CO_2H	38.17	27.94	25.35	23.73	185.2

TABLE 16

α- CARBON ^{13}C CHEMICAL SHIFT INCREMENTS (p.p.m.)

	Substituent						
	H	Me	CH_2OH	OH	CO_2H	Cl	NO_2
t-Butyl	0	2.7	7.7	4.35	13.5	40.1	60.0
Bicyclo [2.2.2] oct-1-yl	0		7.75	44.4	14.5	42.3	
Adamantan-1-yl	0	1.3	6.1	38.9	11.8	38.6	55.7
4-Tricyclyl	0	1.45	7.2	38.1	11.0	27.7	47.9

TABLE 17

β- CARBON CHEMICAL SHIFTS AND SUBSTITUENT INCREMENTS (p.p.m.)

	Substituent						
	H	Me	Cl	OH	CH_2OH	COOH	NO_2
t-Butyl	24.3	31.5	33.6	31.6	26.6	26.3	26.9
C(1)	0	7.2	9.3	7.3	2.3	2.0	2.6
Bicyclo 2.2.2. oct-1-yl	26.81		36.95	33.91	27.78	27.90	
C(2)	0		10.14	7.10	0.97	1.1	
Adamantan-1-yl	38.0	44.6	48.0	45.8	39.4	38.7	40.8
C(2)	0	6.6	10.0	7.8	1.4	0.7	2.8
4-Tricyclyl	31.3	38.2	39.3	36.1	33.8	35.1	35.2
C(3),C(5)	0	6.9	8.0	4.8	2.5	3.8	3.9

TABLE 18

C.N.D.O/2 EXCESS ELECTRON DENSITIES (x 10^4) OF 1-SUBSTITUTED ADAMANTANES.

Substituent	C(1)	(C2)	C(3)	C(4)
H	354	166	354	166
CH_3	460	155	326	170
CH_2OH	295	180	325	170
COOH	-128	254	328	166
NH_2	1201	12	347	158
OH	1722	-76	365	146
F	2246	-142	377	131
Cl	1100	172	350	145
NO_2	626	123	359	134

TABLE 19

C.N.D.O./2 EXCESS ELECTRON DENSITIES (10^4) OF 4-SUBSTITUTED TRICYCLENES.

Substituent	C(1)	C(2) C(6)	C(3) C(5)	C(4)	C(7)	C(8) C(9)	C(10)
H	395	-11	128	415	453	-163	-177
Ml	376	-27	90	550	412	-172	-174
CH_2OH	378	-26	127	375	452	-191	-174
COOH	388	-23	212	-58	545	-216	-178
Cl	400	-16	158	1128	507	-171	-174
OH	396	-10	-109	1779	252	-134	-171
NH_2	386	-21	-43	1296	545	-148	-173
NO_2	422	-1	124	610	606	-134	-179

TABLE 20

PROTONATION SHIFTS (p.p.m.) OF 1-AMINOADAMANTANE AND 1-AMINOCYCLOHEXANE.

	C(1)	C(2)	C(3)	C(4)	Ref.
1-aminoadamantane	-5.0	6.4	0.7	-1.1	91
1-aminocyclohexane	0.4	-4.3	-0.2	-0.5	76

TABLE 21

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 1-SUBSTITUTED CAMPHENES

Substituents	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
H	48.2	165.9	41.7	47.0	23.8	28.9
CH_3	49.9	169.2	42.8	47.4	25.5	35.6
NH_2	66.5	168.2	42.4	45.5	25.3	35.3
OH	84.7	165.9	42.0	44.1	24.9	33.6
Cl	73.4	163.0	42.7	44.9	25.7	37.9
CH_2OH	56.2	165.2	43.3	47.0	24.6	31.0
CO_2H	59.5	162.4	42.9	47.4	24.5	31.9
$CONH_2$	60.7	163.9	43.0	47.7	24.6	31.4
CO_2CH_3	59.7	163.0	42.8	47.3	24.5	31.9
NO_2	96.2	158.8	43.0	44.7	24.7	32.2

	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)
H	37.4	99.1	29.4	25.8		
CH_3	44.3	96.8	29.6	26.1	18.3	
NH_2	45.5	97.2	29.6	26.3		
OH	43.4	97.7	29.4	26.3		
Cl	46.3	101.3	29.8	26.3		
CH_2OH	39.6	98.3	29.2	25.9	63.8	
CO_2H	40.7	101.0	29.6	26.0	180.7	
$CONH_2$	41.6	101.0	29.6	26.0		
CO_2CH_3	40.6	100.6	29.6	26.0	174.1	47.3
NO_2	41.1	101.0	29.6	26.1		

TABLE 22

^{13}C CHEMICAL SHIFT INCREMENTS (p.p.m.) OF 1-SUBSTITUTED CAMPHENES

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)
H	0	0	0	0	0
CH_3	1.7	3.3	1.1	0.4	1.7
NH_2	18.3	2.3	0.7	-1.5	1.5
OH	36.5	0	0.3	-2.9	1.1
Cl	25.2	-2.9	1.0	-2.1	1.9
CH_2OH	8.0	-0.7	1.6	0.0	0.8
COOH	11.3	-3.5	1.2	0.4	0.7
$CONH_2$	12.5	-2.0	1.3	0.7	0.8
CO_2CH_3	11.5	-2.9	1.1	0.3	0.7
NO_2	48.0	-7.1	1.3	-2.3	0.9

	C(6)	C(7)	C(8)	C(9)	C(10)
H	0	0	0	0	0
CH_3	6.7	6.9	-2.3	0.2	0.3
NH_2	6.4	8.1	-1.9	0.2	0.5
OH	4.7	6.0	-1.4	0.0	0.5
Cl	9.0	8.9	2.2	0.4	0.5
CH_2OH	2.1	2.2	-0.8	-0.2	0.1
COOH	3.0	3.3	1.9	0.2	0.2
$CONH_2$	2.5	4.2	1.9	0.2	0.2
CO_2CH_3	3.0	3.2	1.5	0.2	0.2
NO_2	3.3	3.7	1.9	0.2	0.3

TABLE 23

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 4-SUBSTITUTED CAMPHORS.

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)
H	57.4	218.4	43.1	43.2	27.0
Me	59.8	218.9	49.0	45.5	34.4
NH_2	59.0	215.9	49.0	61.9	34.6
OH	58.5	215.7	48.1	79.7	33.2
CO_2H	54.7	215.7	45.3	60.3	30.4
$CONH_2$	55.4	215.8	45.6	60.3	30.7
Cl	57.9	212.3	50.2	70.1	36.2
Br	56.8	213.3	52.1	64.1	37.5
NO_2	60.3	209.8	46.1	91.9	31.2
CO_2Me	60.0	215.4	45.4	54.8	30.4
COMe	60.5	215.7	45.4	60.9	30.6

	C(6)	C(7)	C(8)	C(9)	C(10)
H	29.9	46.6	19.7	19.1	9.2
Me	29.7	48.1	15.9	15.4	10.0
NH_2	28.5	48.2	16.9	15.0	10.4
OH	27.9	48.1	17.0	15.1	10.0
CO_2H	29.1	50.8	18.2	17.2	9.4
CO_2NH_2	29.2	50.4	18,3	17.3	9.6
Cl	28.6	50.6	17.3	15.8	10.4
Br	29.2	51.0	17.9	16.7	10.4
NO_2	27.7	51.8	17.5	16.3	9.6
CO_2Me	29.1	50.6	18.3	17.2	9.5
COMe	29.3	50.5	18.3	17.3	9.3

TABLE 24

^{13}C CHEMICAL SHIFT INCREMENTS (p.p.m.) OF 4-SUBSTITUTED CAMPHORS.

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)
H	0	0	0	0	0
Me	2.4	0.5	5.9	2.3	7.4
NH_2	1.6	-2.5	5.9	18.7	7.6
OH	1.1	-2.7	5.0	36.5	6.2
CO_2H	-2.7	-2.7	2.2	17.1	3.4
$CONH_2$	-2.0	-2.6	2.5	17.1	3.7
Cl	0.5	-5.6	7.7	26.9	9.2
Br	-0.6	-5.1	9.0	20.9	10.5
NO_2	2.9	-8.6	3.0	48.7	4.2
CO_2Me	2.6	-3.0	2.3	11.6	3.4
COMe	3.1	-2.7	2.3	17.7	3.6

	C(6)	C(7)	C(8)	C(9)	C(10)
H	0	0	0	0	0
Me	-0.2	1.5	-3.8	-3.7	0.8
NH_2	-1.4	1.6	-2.8	-4.1	1.2
OH	-2.0	1.5	-2.7	-4.0	0.8
CO_2H	-0.8	4.2	-1.5	-2.0	0.2
$CONH_2$	-0.7	3.8	-1.4	-1.8	0.4
Cl	-1.3	4.0	-2.4	-3.4	1.2
Br	-0.7	4.4	-1.8	-2.4	1.2
NO_2	-2.2	5.2	-2.2	-2.9	0.4
CO_2Me	-0.8	4.0	-1.4	-1.8	0.3
COMe	-0.6	3.9	-1.4	-1.9	0.1

TABLE 25.

C.N.D.O./2 EXCESS ELECTRON DENSITIES ($\times 10^4$) OF 4-SUBSTITUTED CAMPHORS.

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)
H	36	2500	-535	303	-243
CH_3	36	2478	-552	529	-285
NH_2	38	2504	-704	1280	-417
OH	41	2530	-798	1771	-483
NO_2	56	2536	-611	595	-212
COOH	39	2484	-455	-84	-151
Cl	40	2517	-529	1102	-216

	C(6)	C(7)	C(8)	C(9)	C(10)
H	91	521	-237	-223	-177
CH_3	78	480	-240	-227	-175
NH_2	91	365	-218	-204	-173
OH	97	314	-208	-194	-172
NO_2	66	571	-287	-274	-180
COOH	68	609	-276	-263	-176
Cl	65	573	-241	-228	-175

TABLE 26

^{13}C CHEMICAL SHIFTS† (p.p.m.) OF DEUTERATED, NORCAMPHORS AND 4-SUBSTITUTED CAMPHORS AND, IN PARENTHESES, ISOTOPE SHIFTS

a) Norcamphors.

	C(2)	C(3)	C(4)	C(5)
3-exo-d_1	217.88 (-0.07)	44.90 (-0.35)	35.25 (-0.09)	27.19 (-0.05)
3,3-d_2	218.13 (0.25)		35.17 (-0.08)	27.16 (-0.03)

b) 3,3 dideuterio 4-substituted camphors.

Substituent	C(2)	C(3)	C(4)	C(5)
NO_2	210.47 (0.67)	45.34 (-0.63)	90.97 (-0.15)	31.02 (-0.10)
Cl	212.86 (0)	50.22 (-0.62)	69.94 (-0.15)	33.17 (-0.10)
CH_3	218.83 (0.12)	48.03 (-0.94)	45.31 (-0.14)	34.32 (-0.06)

† For carbon atoms where difference between the chemical shift for the deuterated and undeuterated derivatives was found to be greater than experimental error.

TABLE 27.

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 4-SUBSTITUTED CAMPHOR NITRIMINES

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)
H	54.3	189.4	35.2	43.5	31.7
CH_3	55.8	188.7	40.8	46.3	33.9
Cl	53.3	184.5	42.8	70.0	35.8
CO_2H	53.0	185.7	37.5	56.7	31.0
NO_2	55.8	182.3	38.2	91.4	31.0
	C(6)	C(7)	C(8)	C(9)	C(10)
H	26.8	48.9	19.4	18.7	10.3
CH_3	31.3	50.1	16.0	15.0	11.1
Cl	30.6	52.1	16.8	15.8	11.5
COOH	30.3	55.3	17.9	17.1	10.6
NO_2	30.0	53.6	17.2	16.4	10.8

TABLE 28.

^{15}N CHEMICAL SHIFTS (p.p.m.) OF DIAZOALKANES AND RELATED COMPOUNDS.

Compound	N(1)	N(2)	N(3)	ref.
3-diazoacamphor	249	383		This work
9-diazofluorene	266	420		This work
diazomethane H_3C-N(1)-N(2)	-	376		200
Methyl azide H_3C-N(3)-N(1)-N(2)	226	184.5	34	21
azide ion N(2)-N(1)-N(3)	226	77	77	21
Nitrousoxide	216	132		21
nitrogen	284			21
Thiocyanate ion		189		21
cyanate ion		66		21
nitronium ion	224			21

Shifts are in p.p.m. downfield from external NH_4^+

TABLE 29.

C.N.D.O./2 EXCESS ELECTRON DENSITIES (x 10^4) IN DIAZOALKANES AND RELATED COMPOUNDS.

a) Methylene carbons	$\pi(p_z)$	σ
Ketene	-3321	622
Allene	-5288	1120
Diazomethane	-4856	2279

b) π electron density on nitrogens ($p_z + p_y$)

Compound	Central nitrogen	terminal nitrogen
Diazomethane	-2416[a]	-2894[b]
Methyl azide	-1380[a]	-3039[b]
Nitrous oxide	-506[a]	-4082[b]
Nitronium ion	1768	-
Nitrogen	0	0
Cyanate	-	-6480
Isothiocyanate	-	-3072
Azide ion	-1138[a]	-9432[b,c]

a) N(1) b) N(2) c) N(3) see Table 28.

TABLE 30.

LOWEST ENERGY TRANSITIONS FROM ABSORPTION SPECTRA OF DIAZOALKANES AND RELATED COMPOUNDS.

Compound	$\lambda_{max.}$ n.m.	Solvent	Ref.
Diazofluorene	493	MeOH	a
Diazocamphor	403	MeOH	a
Diazomethane	395	Hexane	b
Nitrogen	337	-	c
Nitrous oxide	290	-	d
Methyl azide	287	MeOH	e
Isocyanate ion	300	H_2O	f
Isothiocyanate ion	300	H_2O	g
Azide ion	225	H_2O	h

a) this work
b) Ref.223
c) Ref.224
d) Ref.225
e) Ref.226
f) Ref.227
g) Ref.228
h) Ref.229

TABLE 31

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 4-SUBSTITUTED 1′, 1′, 1′-TRIMETHYLAMMONIO 2′-BENZIMIDES.

Substituent	C(1)	C(2)	C(3)	C(4)	C(7)	C(8)
H	138.52	127.25	127.49	129.14	170.31	55.47
Me	135.58	127.24	128.18	139.00	170.41	55.48
OMe	131.14	128.76	112.74	160.47	170.11	55.53
NMe_2	126.42	128.63	111.39	151.62	170.90	55.64
F	134.70[a]	129.33[b]	114.18[c]	163.56[d]	169.41	55.53
Cl	137.07	128.79	127.54	134.99	169.22	55.51
Br	137.81	129.27	130.62	123.55	169.36	55.50
CN	143.50	128.24	131.52	112.49	168.42	55.59
NO_2	144.97	128.30	122.68	148.28	168.00	55.53
CF_3	142.61	127.97	124.60[e]	130.96[f]	169.10	55.55

a) $^4J_{C-F}$ = 2.7 Hz.

b) $^3J_{C-F}$ = 8.2 Hz.

c) $^2J_{C-F}$ = 24.1 Hz.

d) $^1J_{C-F}$ = 247.2 Hz.

e) $^3J_{C-F}$ = 3.5 Hz.

f) $^2J_{C-F}$ = 31.8 Hz.

Table 32 ^{13}C Chemical Shifts (p.p.m.) of 3-Substituted 1',1',1'-Trimethylammonio 2'-Benzimides

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)
H	138.52	127.25	127.49	129.14	127.49	127.25	170.31	55.47
Me	138.69	128.04	137.00	129.96	127.55	124.52	170.53	55.39
OMe	140.38	112.16	159.26	115.84	128.60	119.97	170.15	55.44
F	141.51[a]	114.39[b]	162.54[c]	116.02[d]	129.09	123.16[e]	169.09	55.50
Cl	140.81	127.71	133.58	129.30	128.98	125.36	169.03	55.54
Br	140.98	130.81	121.88	132.25	129.39	126.18	168.83	55.54
CN	140.38	131.23	111.46	132.56	128.68	131.96	168.01	55.60
NO_2	140.90	122.61	147.87	123.86	128.58	133.64	167.73	55.60
CF_3	139.87	124.53[f]		125.86[g]	128.19	130.96	168.82	

a) $^3J_{C-F}$=7.1Hz; b) $^2J_{C-F}$=22.2Hz; c) $^1J_{C-F}$=162.54Hz; d) $^2J_{C-F}$=21.2Hz;

e) $^4J_{C-F}$=1.9Hz; f) $^3J_{C-F}$=3.5Hz; g) $^3J_{C-F}$=3.2Hz

TABLE 33.

^{13}C CHEMICAL SHIFTS (p.p.m.) OF PARA-SUBSTITUTED 1′, 1′-DIMETHYL 2′- BENZOYHYDRAZIDES.

Substituent	C(1)	C(2)	C(3)	C(4)	C(7)	C(8)
H	133.84	127.28	128.35	131.30	165.89	47.27
Me	130.84	127.09	128.82	141.49	165.60	47.31
OMe	126.09	129.12	113.57	161.12	165.45	47.41
NMe_2	120.44	128.82	110.97	152.47	166.11	47.52
F	(130.26[a,g]	129.84[b,g])	115.30[c]	164.46[d]	164.57	47.39
Cl	132.01	128.36	128.60	137.34	164.66	47.15
Br	132.65	128.92	131.57	126.05	165.00	47.27
CN	137.93	128.27	132.17	114.74	164.14	47.11
NO_2	139.45	128.43	123.71	149.64	163.80	47.36
CF_3	137.26	127.84	125.48[e]	133.26[f]	164.71	47.30

a) $^4J_{C-F}$ = 2.5Hz.

b) $^3J_{C-F}$ = 8.6Hz.

c) $^2J_{C-F}$ = 22.1Hz.

d) $^1J_{C-F}$ = 251.7Hz.

e) $^3J_{C-F}$ = 3.1Hz.

f) $^2J_{C-F}$ = 32.9Hz.

g) Values obtained in 85% CCl_4: 15% $(CD_3)_2CO$ to permit resolution of peaks which in $CDCl_3$ constituted an unresolved absorption between 129.21 and 129.56 p.p.m.

Table 34 ^{13}C Chemical Shifts (p.p.m.) of 3-Substituted 1',1'-Dimethyl 2'-Benzoylhydrazides

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)
H	133.84	127.28	128.35	131.30	128.35	127.28	165.89	47.27
Me	133.85	128.00	138.11	132.05	128.21	124.22	166.08	47.28
MeO	135.27	112.58	159.72	117.66	129.45	119.05	165.68	47.38
F	136.13[a]	114.66[b]	162.54[c]	118.30[d]	130.03[e]	122.95	164.71	47.13
Cl	135.65	127.67	134.48	131.32	129.70	125.51	164.68	47.27
Br	135.84	130.27	122.49	134.29	129.89	125.82	164.54	47.20
CN	135.04	131.17	112.47	134.60	129.49	131.97	163.71	47.21
NO_2	135.44	122.05	148.09	126.90	129.84	133.64	163.48	47.39
CF_3	134.83	124.54[f]	130.94[g]	127.98[h]	129.07	130.74	164.77	47.29
NMe_2	134.65	111.45	150.69	114.11	129.03	115.75	166.59	47.49

a) $^3J_{C-F}$=6.7Hz; b) $^2J_{C-F}$=22.9Hz; c) $^1J_{C-F}$=247.2Hz; d) $^3J_{C-F}$=21.0Hz;

e) $^3J_{C-F}$=7.7Hz; f) $^3J_{C-F}$=3.5Hz; g) $^2J_{C-F}$=32.9Hz; h) $^3J_{C-F}$=3.2Hz

TABLE 35.

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 4-SUBSTITUTED ACETOPHENONES

Substituent	C(1)	C(2)	C(3)	C(4)	C(7)	C(8)
H	137.23	128.59	128.31	133.10	198.00	26.52
Me	134.79	128.78	129.23	143.78	197.59	26.38
MeO	130.57	130.57	113.71	163.55	196.55	26.22
NMe_2	125.46	130.52	110.65	153.27	196.30	25.93
F	133.81[a]	131.02[b]	115.74[c]	165.85[d]	196.30	26.42
Cl	135.54	129.72	128.88	139.51	196.63	26.47
Br	135.88	129.81	131.84	128.19	196.70	26.42
NO_2	141.54	129.38	123.86	(153.6[e])	196.38	26.94
CF_3	139.78	125.62	128.88[g]	-	196.95	26.78
Ph	135.94	128.92	127.21	145.73	197.55	26.54

a) $^4J_{C-F}$ = 3.5 Hz.
b) $^3J_{C-F}$ = 9.0 Hz.
c) $^2J_{C-F}$ = 21.5 Hz.
d) $^1J_{C-F}$ = 253.9 Hz.
e) visual assignment

g) $^3J_{C-F}$ = 3.6 Hz.

Table 36 ^{13}C Chemical Shifts (p.p.m.) of 3-Substituted Acetophenones

Substituent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)
H	137.23	128.59	128.31	133.10	128.31	128.59	198.00	26.52
Me	137.33	128.81	138.33	133.81	128.47	125.61	198.13	26.54
OMe	138.62	112.52	159.94	119.54	129.58	121.10	197.74	26.63
NMe_2	138.08	110.92	150.71	117.00	129.52	116.97	198.49	26.71
F	134.36	114.96	162.97	120.09	130.33	124.18	196.56	26.59
Cl	138.62	128.36	134.90	133.00	129.93	126.42	196.60	26.58
Br	138.89	131.37	122.97	135.94	130.18	126.85	196.51	26.55
NO_2	138.36	123.13	148.54	127.88	130.05	133.93	195.75	26.71
CF_3	137.67	- [f]	- [f]	- [f]	- [f]	- [f]		

a) $^3J_{C-F}$=6.3Hz; b) $^2J_{C-F}$=22.1Hz; c) $^1J_{C-F}$=247.5Hz; d) $^2J_{C-F}$=21.9Hz;

b) $^4J_{C-F}$=2.7Hz f) not assigned

TABLE 37

^{13}C CHEMICAL SHIFTS (p.p.m.) OF C(7),C(8) IN PARA SUBSTITUTED TRIPHENYLPHOSPHONIUM AND TRIPHENYLARSONIUM YLIDES

	Triphenylphosphonium ylides		Triphenylarsonium ylides	
Substituent	C(7)	C(8)	C(7)	C(8)
H	184.80	50.54	181.80	57.13
Me	185.06	50.03	181.75	56.59
MeO	182.71	50.12	179.71	56.54
F	183.56	50.47	180.67	56.88
Cl	183.56	50.98	180.31	57.43
Br	183.57	50.98	180.40	57.48
CN	182.14	52.93	179.01	59.23
NO_2	181.87	53.55	178.76	59.90
Ph	-	-	180.56	57.35

TABLE 38.

C.N.D.O./2 EXCESS ELECTRON DENSITIES (q_Z),(q_σ) and π BOND ORDERS (p_Z)($\times 10^4$) OF META AND PARA SUBSTITUTED 1', 1', 1' TRIMETHYLAMMONIO 2'-BENZIMIDES RELATIVE TO UNSUBSTITUTED (181)

a) para substituents

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	33	22	0	8	0	-37	-50	-74
q_σ C(7)	-13	0	+22	-6	0	30	44	71
p_ZC(1)-C(7)	-47	-38	-20	-20	0	2	15	21

b) meta substituents

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	-10	-21	-37	-6	0	-30	-40	-61
q_σ C(7)	-12	6	32	2	0	47	51	80
p_ZC(1)-C(7)	17	19	21	10	0	12	15	20

TABLE 39

C.N.D.O./2 EXCESS ELECTRON DENSITIES AND π BOND ORDERS (x 10^4) OF PARA SUBSTITUTED STYRENES RELATIVE TO UNSUBSTITUTED STYRENE

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	68	45	-1	24	0	-70	-93	-142
q_σ C(7)	-13	1	+22	-5	0	34	51	68
p_ZC(1)-C(7)	27	19	9	16	0	21	13	25
q_Z C(8)	-168	-129	-37	-57	0	113	175	265
p_ZC(7)-C(8)	14	10	4	8	0	6	2	7

TABLE 40.

C.N.D.O./2 EXCESS ELECTRON DENSITIES AND π BOND ORDERS (x 10^4) OF META AND PARA-SUBSTITUTED ACETOPHENONES RELATIVE TO UNSUBSTITUTED ACETOPHENONE

a) para substituents

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	41	26	5	14	0	-37	-52	-81
q_σ C(7)	-11	-2	23	-6	0	35	42	75
p_ZC(1)-C(7)	-70	-56	-30	-30	0	4	24	32
q_Z C(8)	12	7	-2	5	0	-11	-17	-26
q_σ C(8)	-15	-13	-5	-6	0	8	13	20

b) meta substituents

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	-10	-18	-41	-2	0	-35	-41	-66
q_σ C(7)	-8	6	31	-4	0	38	47	72
p_ZC(1)-C(7)	19	20	26	9	0	15	19	27
q_Z C(8)	3	-4	-19	2	0	-19	-23	-37
q_σ C(8)	3	7	15	0	0	11	15	24

TABLE 41.

C.N.D.O./2 EXCESS ELECTRON DENSITIES AND π BOND ORDERS (x 10^4) OF PARA-SUBSTITUTED PHOSPHONIUM YLIDES RELATIVE TO UNSUBSTITUTED (182)

	NMe_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z C(7)	34	23	1	14	0	-43	-49	-83
q_σ C(7)	-22	-11	9	-6	0	24	38	54
p_ZC(1)-C(7)	-80	-64	-33	-34	0	8	31	41
q_Z C(8)	-7	-13	-25	+2	0	-23	-21	-41
q_σ C(8)	-14	-12	8	1	0	6	-7	0

TABLE 42.

C.N.D.O./2 EXCESS ELECTRON DENSITIES AND π BOND ORDERS (x 10^4) OF PARA-SUBSTITUTED NITROBENZENES RELATIVE TO UNSUBSTITUTED NITROBENZENE

	NH_2	OMe	F	Me	H	Cl	CF_3	NO_2
q_Z N	47	20	0	16	0	-37	-54	-83
q_σ N	-18	2	29	-15	0	39	48	83
p_ZC(1)-N	59	35	23	27	0	0	17	24

TABLE 43

CORRELATIONS OF ^{13}C S.C.S. IN PARA SUBSTITUTED AROMATIC SYSTEMS WITH F AND R.

	f	r	%R	c[a]
C(7) (78)-(88)	-1.56	-1.09	30.4	0.983
C(7) (97)-(106)	-1.15	-0.98	34.7	0.952
C(7) (116)-(125)	-1.32	1.43	-36.5	0.853
C(7) (116)-(125) excluding (124)	-1.31	1.0	-43.3	0.966
C(8) (116)-(125)	0.17	0.87	76.2	0.971
C(7) (134)-(141)	-2.42	0.69	-21.6	0.643
C(8) (134)-(141)	1.57	3.11	55.8	0.925
C(7) (142)-(150)	-1.96	0.64	-25.6	0.640
C(8) (142)-(150)	1.12	4.11	69.6	0.949

a) c = correlation coefficient.

TABLE 44.

CORRELATIONS OF EXCESS ELECTRON DENSITIES AND π BOND ORDERS IN PARA-SUBSTITUTED AROMATIC SYSTEMS WITH F AND R.

	f	r	%R	C
q_Z C(7)(78)-(88)	-0.0044	-0.0080	53.2	0.947
p_ZC(1)-C(7)(116)-(125)	0.0017	0.0067	71.1	0.986
q_Z C(7)(116)-(125)	-0.0049	-0.0089	53.2	0.954
q_Z C(7)(134)-(141)	-0.0054	-0.0082	48.9	0.947

TABLE 45.

CORRELATIONS OF ^{13}C S.C.S. AND EXCESS ELECTRON DENSITIES IN META-SUBSTITUTED AROMATIC SYSTEMS, WITH F AND R.

	f	r	%R	C
C(7)S.C.S.(89)-(96)	-2.10	-1.46	30.3	0.985
C(7)S.C.S.(106)-(115)	-1.82	-0.99	25.4	0.982
C(7)S.C.S.(125)-(133)	-1.94	-1.03	24.9	0.977
q_Z C(7) (125)-(133)	-0.0044	0.0005	-6.6	0.928

Table 46.

C.N.D.O./2 EXCESS ELECTRON DENSITIES (x 10^4) IN META-SUBSTITUTED ANILINES RELATIVE TO UNSUBSTITUTED ANILINE.

	NMe_2	OMe	Me	H	F	Cl	CF_3	NO_2
q_Z N	15	14	6	0	12	-2	1	-3
q_σ N	-18	-12	-8	0	4	27	27	44
q_{total} N	-3	2	-2	0	16	25	28	41

TABLE 47

^{13}C CHEMICAL SHIFTS (p.p.m.) OF PARA-SUBSTITUTED 1′, 1′, 1′ TRIMETHYLAMMONIO 2′-CINNAMIMIDES.

Substituent	C(1)	C(2)	C(3)	C(4)	C(7)	C(8)	C(9)
H	136.13	126.97	128.21	127.91	135.52	125.88	170.1
F	132.75[a]	128.80[b]	115.51[c]	162.38[d]	134.19	126.43	170.1
NMe_2	124.71	128.47	112.10	150.49	135.97	121.37	171.2
OMe	129.31	128.59	114.02	159.77	135.32	124.02	170.8
Me	133.65	127.13	129.27	138.11	135.43	125.35	170.4
Cl	135.13	128.45	128.72	133.71	134.31	127.16	170.1
CN	141.17	127.66	132.37	111.11	133.63	130.45	169.5
NO_2	143.19	127.76	123.97	147.24	133.20	131.35	169.5

a) $^4J_{C-F}$ = 2.5 Hz. b) $^3J_{C-F}$ = 8.3 Hz.

c) $^2J_{C-F}$ = 21.8 Hz. d) $^1J_{C-F}$ = 247.5 Hz.

TABLE 48

C.N.D.O./2 EXCESS ELECTRON DENSITIES AND π BOND ORDERS ($\times 10^4$) OF PARA SUBSTITUTED 1′, 1′, 1′ TRIMETHYLAMMONIO 2′-CINNAMIMIDES RELATIVE TO UNSUBSTITUTED (183)

	NMe_2	OMe	F	Me	H	Cl	NO_2
q_Z C(7)	84	54	6	27	0	-91	-193
q_Z C(8)	-169	-123	-29	-54	0	134	294
q_Z C(9)	19	11	-3	6	0	-23	-47
p_ZC(1)-C(7)	-33	-24	-12	-20	0	-24	-29
p_ZC(7)-C(8)	19	13	5	10	0	5	4
p_ZC(8)-C(9)	-20	-12	-3	-8	0	11	24

TABLE 49

^{13}C CHEMICAL SHIFTS (p.p.m.) OF 1′, 1′, 1′ TRIMETHYLAMMONIO 2′-PHENYLACETIMIDES.

Substituent	C(1)	C(2)	C(3)	C(4)	C(7)	C(8)
H	138.96	129.10	128.07	125.78	43.51	174.91
Me	135.79	128.96	128.80	135.10	43.02	175.12
MeO	131.14	130.00	113.69	158.00	42.51	175.21
F	134.67[a]	130.45[b]	114.71[c]	161.48[d]	42.59	174.71
Cl	137.43	131.54	130.51	131.54	42.78	174.41
Br	137.88	130.94	131.09	119.73	42.86	174.71
NO_2	147.07	130.00	123.24	146.49	43.56	173.37

a) $^4J_{C-F}$ = 3.2 Hz ; b) $^3J_{C-F}$ = 7.7 Hz ;

c) $^2J_{C-F}$ = 21.0 Hz ; d) $^1J_{C-F}$ = 247 Hz.

TABLE 50.

C.N.D.O./2 EXCESS ELECTRON DENSITIES (10^4) OF PARA SUBSTITUTED 1′,1′,1′ TRIMETHYLAMMONIO 2′-PHENYLACETIMIDES RELATIVE TO UNSUBSTITUTED (184)

	NMe_2	OMe	F	Me	H	Cl	NO_2
q_Z C(7)	31	16	-12	11	0	-43	-87
q_σ C(7)	5	16	34	0	0	32	49
q_{total} C(7)	36	32	22	0	0	-11	-28
q_Z C(8)	-16	-9	3	-4	0	22	45
q_σ C(8)	1	-5	-10	0	0	-17	-33
q_{total} C(8)	-15	-14	-7	-4	0	5	12

TABLE 51

CORRELATION OF ^{13}C S.C.S. IN 1′, 1′, 1′ TRIMETHYLAMMONIO 2 -CINNAMIMIDES AND 2 -PHENYLACETIMIDES WITH F AND R.

	f	r	%R	C
C(7)(151)-(158)	-1.57	-1.39	35.6	0.985
C(8)(151)-(158)	3.00	7.51	60.9	0.997
C(9)(151)-(158)	-0.55	-1.23	58.2	0.973
C(7)(159)-(165)	-0.07	2.10	94.9	0.867
C(8)(159)-(165)	-0.86	-1.50	51.5	0.939

TABLE 52.

PROTON-PROTON COUPLING CONSTANTS IN 4-SUBSTITUTED CAMPHORS AND CAMPHORNITRIMINES.

	$^4J_{H3\ exo - H5\ exo}$		$^2J_{H3exo-H3\ endo}$
Substituent	Camphors	Camphornitrimines	Camphors.
CH_3	2.33	2.20	18.44
CH_2OH	2.52		18.30
OH	3.08		18.20
CO_2H	3.26	3.03	18.59
$COCH_3$	3,40		17.96
$CONH_2$	3.35		18.05
Cl	3.50		18.20
Br	3.53		18.31
NO_2	3.85	3.65	18.30

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APPENDIX

	Bond orders ($\times 10^4$)
Ylide (181)	2397
Acetephenone (125)	2676
Styrene (11)	2962
Phosphonium Ylide (182)	2796
Nitrobenzene	2151